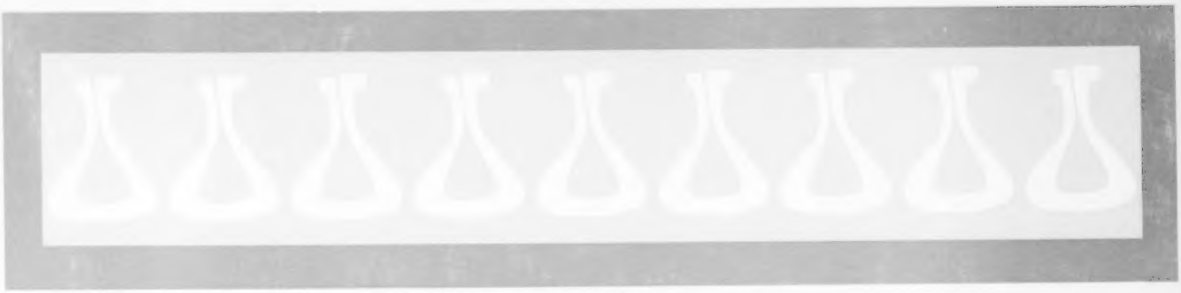

THE NATIONAL CLEARINGHOUSE FOR MENTAL HEALTH INFORMATION

VOL. 12 NO. 1 July 1974

PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

168801 Palazzo, G. Research Laboratories, Aziende Chimiche Riunite Angelini Francesco, Rome, Italy **Chemistry of trazodone.** Current Threapeutic Research. 15(10S):745-748, 1973.

The chemistry of trazodone is reported. Chemically Trazodone (I) is 2-(93-(4-(m.chlorophenyl)-1-piperazinly)propyl))s.trazolo(4,3-a) pyridin-3(2H)one. It is the first s.triazolo(4,3-a)pyridine derivative which has been used in therapy and several derivatives of that nucleus are described. Reports concern oxidation states, observations in the ultraviolet spectra, in the NMR spectra, behavior toward alkali and in alkylation reactions. A study of the metabolism of the drug is in progress. 7 references.

169073 Frigerio, Alberto; Baker, Kenneth M.; Morselli, Paolo L. Istituto di Ricerche Farmacologiche 'Mario Negri,' Milano, Italy **Gas chromatographic - mass spectrometric studies on tricyclic psychotropic drugs.** Psychopharmacology Bulletin. 9(4):34, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the technique of gas chromatography mass spectrometry was described in the study of the metabolism and plasma levels of tricyclic psychotropic drugs. A description of the study and identification of the metabolites of carbanazepine using this technique is given. The gas chromatographic degradation of carbamazepine and its metabolites are described. Data on the quantitative determination of imipramine in the plasma of depressed patients undergoing chronic treatment by the mass fragmentography technique is given. (Journal abstract modified)

169074 Bertilsson, Leif; Sjoqvist, Folke. Dept. of Clinical Pharmacology, Karolinska Institutet, Huddinge University Hospital, Huddinge, Sweden **Mass fragmentography in clinical psychopharmacology.** Psychopharmacology Bulletin. 9(4):35-36, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, applications in clinical psychopharmacology of the mass fragmentography technique to metabolic and pharmacokinetic studies on the trycyclic antidepressant drug nortriptyline in man and the study of biogenic amine metabolites in the cerebrospinal fluid of depressed patients were discussed. It is noted that the combination of clinical ratings scales, pharmacokinetic methods, and specific analytical methods are prequisites to elucidate mechanisms of action of antidepressant drugs in man and to explore the reasons behind interindividual differences in the response to these drugs. 11 reference. (Journal abstract modified)

169818 Parmar, Surendra S.; Joshi, P. C.; Ali, Basheer; Brumleve, Stanley J. Department of Physiology and Pharmacology, School of Medicine, University of North Dakota, Grand Forks, ND 58201 **Synthesis of substituted cinnamides: relationship between anticonvulsant and monoamine oxidase inhibitory properties.** Journal of Pharmaceutical Sciences. 62(12):1986-1989, 1973.

Alpha-benzoylamino-N-(substituted esters)-substituted cinnamides and their corresponding hydrazides were synthesized and evaluated for anticonvulsant activity. The data seem to indicate a trend of more protection from convulsions with less mortality. Each hydrazide or its precursor ester was found to be devoid not only of the central nervous system depressant effect but also of 24 hour mortality in the 100mg/kg dose administered to experimental mice. The results suggest a greater anticonvulsant activity of alpha-benzoylamino-N-(substituted hydrazides)-substituted cinnamides as compared to their corresponding esters. 10 references.

171971 Martin, Ian L.; Ansell, G. Brian. MRC Neuropharmacology Unit, The Medical School, Birmingham B15 2TJ, England **A sensitive gas chromatographic procedure for the estimation of noradrenaline, dopamine and 5-hydroxytryptamine in rat brain.** Biochemical Pharmacology (Oxford). 22(4):521-533, 1973.

A gas chromatographic method for the estimation of noradrenaline, dopamine and 5-hydroxytryptamine in rat brain is reported. The method utilizes homogenization of the tissue in acid butanol, alumina adsorption of the catecholamines and their subsequent ion pair extraction. This is

combined with the solvent extraction of 5-hydroxytryptamine to produce a method which is sufficiently sensitive to estimate the amount of these amines in discrete areas of a single rat brain. 31 references. (Author abstract)

173589 Rusch, David Neil. Philadelphia College of Pharmacy and Science **The syntheses of 2,3-dihydro-1,4-benzothiazine derivatives. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-24056 HC$10.00 MF$4.00 111 p.

The historical development of phenothiazine drugs was reviewed, and the structural activity characteristics of phenothiazine derivatives were shown to compare favorably with the theoretical model of 1,4-benzothiazine derivatives. The synthetic development of 2,3-dihydro-1,4-benzothiazine is outlined. Two methods were used to prepare 2-(2-aminophenylthio) ethanol from o-aminothiophenol and ethylene oxide or ethylene chlorohydrin, and two other methods were used to prepare 2,3-dihydro-1,4-benzothiazine. The identity of the synthesized 2-(2-aminophenylthio) ethanol and of the synthesized 2,3-dihydro-1,4-benzothiazine was established by NMR data, elemental analyses, and IR data. Substituted o-aminothiophenols were prepared as precursors in the syntheses of substituted 2-(2-aminophenylthio) ethanols and 2,3-dihydro-1,4-benzothiazin-3-ones which in turn are necessary to prepare 6-substituted and 7-substituted, 2-3-dihydro-1,4-benzothiazines. The N-dialkylaminoalkyl derivatives of the substitutde 2,3-dihydro-1,4-benzothiazines were prepared. The preparation of stable salts of these N-dialkylaminoalkyl derivatives presented few difficulties when the side chain contained two aliphatic nitrogen atoms, whereas salts of those derivatives containing a single aliphatic nitrogen in the side chain were exceedingly difficult to prepare. (Journal abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

171301 Houser, Vincent P.; Pare, William P. Pavlovian Research Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **Analgesic potency of sodium salicylate, indomethacin, and chlordiazepoxide as measured by the spatial preference technique in the rat.** Psychopharmacologia (Berlin). 32(2):121-131, 1973.

The analgesic potency of various doses of sodium salicylate indomethacin and chlordiazepoxide were measured using the spatial preference technique. All three agents were active in a wide range of doses indicating that this technique is sensitive to the weak analgesics. The chlordiazepoxide data were interpreted to suggest that this tranquilizing agent may be able to impair the appreciation of the emotional qualities of electric shock, thus reducing the animal's motivation to escape the noxious stimulus. A procedure for computing ED50 estates was also presented along with a summary of the ED50 values for several standard narcotic and narcotic antagonist analgesics. Since this procedure is a reliable and sensitive index of drug induced analgesia, it should be useful as a screening procedure in evaluating the analgesic potency of a wide variety of chemical agents. 11 references. (Author abstract)

173495 Giurgea, C. Department of Pharmacology, UCB, Dipha, Brussels, Belgium **The 'nootropic' approach to the pharmacology of the integrative activity of the brain.** Conditional Reflex. 8(2):108-115, 1973.

A new drug, Piracetam, that interferes with learning and memory is described. Piracetam is an atoxic compound which in dosages such as g/kg does not interfere with autonomic functions, general behavior, level of wakefulness, or the limbic system. In doses such as mg/kg it improves several learning and memory abilities, protects against experimental amnestic agents, facilitates EEG recovery after severe hypoxia and also facilitates interhemispheric transfer. Discussion is made on the basis of the particular neuropharmacology as well as on the available biochemical and human clinical correlations to emphasize the selectivity of the compound on telencephalic integrative mechanisms. Picacetam is presented as the first comer of a new psychotropic class for which the term nootropic is proposed. 18 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

167287 Stull, Richard E.; Jobe, Phillip C.; Geiger, Paul F.; Ferguson, Gary G. College of Pharmacy and Allied Health Professions, Northeast Louisiana University, Monroe, LA 71201 **Effects of dopamine receptor stimulation and blockade on Ro 4-1284-induced enhancement of**

electroshock seizure. Journal of Pharmacy and Pharmacology (London). 25(10):842-844, 1973.

The effects of dopamine receptor stimulation and blockade on Ro 4-1284 induced enhancement of electroshock seizure were studied. Ro 4-1284 produced a marked enhancement of seizure intensity within 2 h after its administration, a time when brain dopamine and noradrenaline are severly depleted in rats. In contrast, central dopamine receptor stimulation by apomorphine or by the intracerebroventricular injection of dopamine itself completely antagonized the enhancing effects of Ro 4-1284. However, pretreatment with pimozide, a dopamine receptor blocking agent, effectively prevents both the apomorphine and the dopamine induced antagonizing effects. The findings indicate that an increase in central dopamine activity diminishes seizure intensity whereas a decrease in such activity enhances seizure intensity. The results indicate that the seizure diminishing actions of dopamine and apomorphine result from a specific dopamine receptor effect. These observations lend further support to the concept that endogenous dopamine exerts an inhibitory effect on electroshock seizure. 12 references.

167325 Kuczenski, Ronald. Dept. of Psychiatry, Univ. of California at San Diego, La Jolla, CA 92037 **Striatal tyrosine hydroxylases with high and low affinity for tyrosine: implications for the multiple-pool concept of catecholamines.** Life Sciences (Oxford). 13(3):247-255, 1973.

The implications for the multiple pool concept of catecholamines are discussed in an examination of striatal tyrosine hydroxylases with high and low affinity for tyrosine. It was found that synaptic membrane - bound tyrosine hydroxylase from rat striatum exhibits a decreased Km for cofactor and a decreased Km for substrate over values obtained for the soluble enzyme. It is suggested that the proximity of this fraction of the catecholamine biosynthetic apparatus to the probable site of neurotransmitter release and its higher affinity for substrate provide for a mechanism by which newly synthesized transmitter may be preferentially released. 28 references. (Author abstract modified)

167326 Volicer, Ladislav; Gold, Barry I. Dept. of Pharmacology, Boston Univ. School of Medicine, Boston, MA 02118 **Effect of ethanol on cyclic AMP levels in the rat brain.** 13(3):269-280, 1973. Life Sciences. (Oxford, England).

The effect of ethanol in cyclic AMP levels in the rat brain was investigated. It was found that ethanol decreased in a dose dependent manner the cyclic AMP level in the rat brain and separation of the brain into several parts showed that this increase was limited to the cerebellum. High doses of ethanol blocked the rise of cyclic AMP levels induced by decapitation in all brain areas studied. Pentobarbital treatment which produced central depression similar to that caused by a high dose of ethanol, also decreased the cyclic AMP level in the cerebellum but it prevented the postdecapitation rise only in the pons and medulla oblongata. Lower doses of ethanol enhanced the decapitation induced rise of cyclic AMP levels in the pons and medulla oblongata. 28 references. (Author abstract modified)

167328 Luckens, Mark M.; Malone, Marvin H. College of Pharmacy, University of Kentucky Medical Center, Lexington, KY 40506 **Cardiovascular effects of reserpine, yohimbine, and reserpine-yohimbine mixtures on intact anesthetized dog.** Journal of Pharmaceutical Sciences. 62(8):1286-1290, 1973.

Cardiovascular and respiratory parameters plus responses to periodically injected epinephrine were monitored for 5 hr. in the anesthetized dog after single intravenous injections of saline, reserpine, yohimbine, or resperpine - yohimbine mixtures. Whole root Rauwolfia serpentina contains reserpine like and yohimbine like alkaloids and is widely used and classified as a reserpine like agent. However, qualitative results in the present study indicate interactions between reserpine and yohimbine when administered concurrently, with end results incorporating the time response profiles of both agents when given singly. 19 references. (Journal abstract)

167329 Lalley, P. M; Rossi, G. V.; Baker, W. W. Department of Pharmacology, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15213 **Tremor induction by intracaudate injections of bretylium, tetrabenazine, or mescaline: functional deficits in caudate dopamine.** Journal of Pharmaceutical Sciences. 62(8):1302-1307, 1973.

Tremor responses evoked by intracaudate injections of tetrabenazine, bretylium, or mescaline in cats with chronically implanted recording electrodes and microinjection cannulas are studied, supporting the hypothesis that an imbalance in the caudate between dopamine inhibition and acetylcholine excitation, in favor of acetylcholine

excitation, results in tremors. The tremors were suppressed by local injections of catecholamines (dopamine and epinephrine), scopolamine, or hemicholinium, but were intensified by intracaudate serotonin. Although local acetylcholine had no effect on established tremor activity, tremors abolished by hemicholinium were reestablished by small doses of acetylcholine. Results suggest that interference with local dopamine inhibitory mechanisms ('functional dopamine deficiency') was the basis for the tremorgenic actions of bretylium, tetrabenazine, and mescaline. Findings also indicate that sustained endogenous acetylcholine activity in the caudate is a necessary condition for the development and maintenance of tremor activity. 21 references. (Journal abstract modified)

167358 Pong, Schwe F.; Graham, Lewis T., Jr. Section of Neurobiology, Institute of Psychiatric Research, Indiana Univ. Medical Center, Indianapolis, IN 46202 **Effect of 6-hydroxydopamine on dark adaptation in the rat retina.** Life Sciences (Oxford). 13(1):15-21, 1973.

The effect of 6-hydroxydopamine (6-HD) on dark adaptation was studied in the rat retina. 6-HD administered iv to light adapted rats appears to prevent the recovery of retinal sensitivity during subsequent dark adaptation through its interaction with the photochemical mechanisms. Results tend to support the hypothesis that the toxicity of 6-HD is mediated through the binding of its oxidation product(s) with nucleophilic groups of biological macromolecules. 27 references. (Author abstract modified)

167359 Dowson, J. H. Dept. of Psychiatry, Royal Edinburgh Hospital, Edinburgh 10, Scotland **Animal models for an enzymic blood-brain barrier mechanism for therapeutically administered L-DOPA.** Life Sciences (Oxford). 13(1):23-29, 1973.

The blood-brain barrier to L-3,4-dihydroxyphenylalanine (L-DOPA) in the rat was compared to that of the cat by incubating tissue from three brain regions in a medium containing L-DOPA and nialamide. The intensity of capillary wall fluorescence in each region was compared with the intensity of the surrounding increased diffuse formaldehyde induced fluorescence which was measured by a microfluorimetric method. Unlike the rat brain capillary walls which showed a marked increase in fluorescence due to uptake of L-DOPA and subsequent dopamine formation and accumulation, the capillary walls of the cat brain samples did not show evidence of dopamine accumulation. The nature of the blood-brain barrier to L-DOPA in man is discussed in relation to the finding. 8 references. (Author abstract modified)

167415 Seliger, Deborah L. Rutgers University, Camden, NJ 08102 **Effect of prenatal maternal administration of d-amphetamine on rat offspring activity and passive avoidance learning.** Physiological Psychology. 1(3):273-280, 1973.

A study was made of Gravid albino rats that were injected subcutaneously with 0, 5, or 10mg/kg body weight of d-amphetamine during days 5-9 or days 12-16 of gestation. Offspring were assessed for activity level and passive avoidance learning. Almost all of the drug groups, especially those whose mothers received 5mg of d-amphetamine early in pregnancy, displayed significantly higher activity than did the controls. Administration of 5mg of d-amphetamine early in pregnancy was also detrimental to the learning of a passive avoidance response in their offspring, but large doses, whether given early or late in pregnancy, did not affect this behavior. 33 references. (Journal abstract modified)

167445 Goodwin, B. L.; Johnson, R. D.; Leask, Barbara G. S.; Ruthven, C. R. J.; Sandler, M. Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, Goldhawk Road, London, W6 OXG, England **Threo-3,4-dihydroxyphenylserine, a poor source of noradrenaline in the rat.** Experientia (Basel). 28(11):1298-1299, 1972.

The major urinary metabolite of noradrenaline in the rat, 4-hydroxy-3-methoxyphenylglycol, was measured after threo-3,4-dihydroxyphenylserine (DOPS) administration. Not more than 20% of administered DOPS could be accounted for. Of this total, a very small proportion consisted of noradrenaline metabolites. It is therefore felt that administered DOPS is a poor in vivo substrate for dopa decarboxylase in the rat. The very small production of noradreline from DOPS was overshadowed by a conversion of DOPS to vanillic acid and related compounds of the order of 10%. Possible reasons for this are given. 31 references.

167449 Etevenon, P.; Boissier, J. R. Unite de Recherche de Neuropsychopharmacologie, INSERM, 2, rue d'Alesia, F-75 Paris 14e, France **LSD effects on signal-to-noise ratio and lateralization of visual cortex and lateral geniculate during**

photic stimulation. Experientia (Basel). 28(11):1338-1340, 1972.

Lysergic acid diethylamide (LSD) effects on signal to noise ratio and lateralization of visual cortex and lateral geniculate body in which photic stimulation was delivered via fiber optics and hemispheric goggles were studied. The subjects were curarized rabbits placed under artificial respiration. Following LSD administration, contralateral stimulation increased signal to noise values as well as lateralization index. After contralateral stimulation, amphetamine increases the lateralization of visual areas, whereas pentobarbital decreased it towards control prestimulation values and ipsilateral stimulation effects. Although the study did not use filtered electroencephalogram (EEG) but did use raw EEG before integration, the results are coherent with previous studies and the technique appears to be valuable in studying drug effects. 10 references. (Author abstract modified)

168130 Moore, Robert Haldane, III. University of Tennessee Medical Units at Memphis **Neuropharmacological analysis of effects of doxepin in rabbits (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-24464 HC$10.00 MF$4.00 131 p.

Central actions of doxepin in conscious adult rabbits were examined, using techniques for obtaining electroencephalograms (EEG) and integrated EEG recordings, to determine the activity of this psychoactive drug and its interaction with methamphetamine and physostigmine electroencephalographically. Doxepin at 0.1mg/kg did not alter electrogenesis, and 0.5mg/kg increased electrogenesis but not to values significantly greater than control. Doses of 1,2, and 5mg/kg evoked significant increases in electrogenesis from their respective control levels for at least 1 hr. Methamphetamine and physostigmine at 1mg/kg and 0.1mg/kg caused a significant decrease in electrogenesis for at least 1 hr. Methamphetamine gradually reduced the increased electrogenesis induced by 1 or 5mg/kg doses of doxepin. Some EEG tolerance also occurred. Activation of the EEG by electrostimulation of the midbrain reticular formation, electrostimulation of the sciatic nerve, and auditory stimulation were inhibited by both doses of doxepin (1 and 5mg/kg), although following either dose, reticular formation stimulation was more effective in producing alerting patterns of the EEG than were the other two types of stimulation. Behaviorally, methamphetamine effects were not greatly affected by doxepin, but bizarre responses occurred in some animals. Findings indicate that doxepin exerts central anticholinergic effects resembling those of atropine. (Journal abstract modified)

168131 Yu, Jia-Huey Lin. University of Michigan **The uptake, retention and metabolism of 3H-5-hydroxytryptamine in brain slices and ileum from the rat: effects of cocaine, desmethylimipramine and reserpine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-24725 HC$10.00 MF$4.00 138 p.

The uptake, retention and metabolism of 3H-5-hydroxytryptamine (3H-5-HT) in slices of rat brain and in isolated ileal strips were studied. Cocaine, a competitive inhibitor of norepinephrine uptake into adrenergic neurons, was used to examine the possibility that 3H-5-HT might be transported into adrenergic neurons. Because desmethylimipramine (DMI) apparently blocks specifically intraneuronal, vesicular transport in the brain, effects of DMI and cocaine on the uptake, retention, and metabolism of 3H-5-HT were examined in the slices and isolated strips. Uptake and binding were not the same in slices from all four areas of the brain: the strips had an affinity for 3H-5-HT and retention similar to that of slices from brainstem, hypothalamus, or cortex, but the V max was much less than that found with any slices. Both cocaine and DMI in vitro markedly inhibited uptake and retention by all tissues. Effects of pretreatment with reserpine and pargyline suggest that a significant amount of 3H-5-HT is oxidatively deaminated at nonneuronal sites, and it appears that 3H-5-HT is taken up selectively by 5-HT-containing neurons in brain slices and in ileal strips, but that uptake mechanisms for 5-HT differ from those for norepinephrine. Extraneuronal metabolism of 5-HT is also important. (Journal abstract modified)

168418 DeFeudis, F. V.; Marks, J. H. Section of Neurobiology, Institute of Psychiatric Research, Indianapolis, IN **Brain to serum distribution of radioactivity of injected (3H)-d-amphetamine in differentially housed mice.** Biological Psychiatry. 6(1):85-88, 1973.

The extent to which radioactivity due to 3H-d-amphetamine enters brain and serum under prolonged periods of environmental change was investigated in mice. Environments were isolated or

aggregated conditions. Findings indicate that this drug is handled similarly in both isolated and aggregated mice, but that the rates of metabolism and excretion are greater in aggregated, hyperactive mice. Differences in these findings and those of previous workers, which indicated that aggregation increased d-amphetamine levels in brain, can be best explained as being due to the different conditions of housing which were employed. It is becoming increasingly evident that actions and dispositions of centrally active drugs are profoundly influenced by environmental conditions. 6 references. (Author abstract modified)

168436 Taber, Curtis A.; Anderson, Edmund G. University of Texas, Department of Pharmacology, Dental Branch, Houston, TX **Paradoxical blockade by p-chlorophenylalanine of 5-hydroxytryptophan facilitatory actions on spinal reflexes.** Journal of Pharmacology and Experimental Therapeutics. 187(2):229-238, 1973.

Cats pretreated with p-chlorophenylalanine (pCPA), given as two injections of 300mg/kg 24 hours apart, were spinalized and prepared for reflex recording 48 to 96 hours after the initial dose. Unexpectedly, pCPA pretreatment completely prevented the usual facilitatory effects of 5-hydroxytryptophan (5-HTP) on the monosynaptic reflex. It is suggested that blockade of the facilitatory effects of 5-HTP by pCPA results from increased retention of newly synthesized 5-hydroxytryptamine (5-HT) by the nearly empty synaptic storage vesicles. This prevents significant overflow of 5-HT onto subsynaptic receptors. Conversely, the potentiating action of reserpine results from blockade of the entry of newly formed 5-HT into synaptic vesicles, thus increasing the synaptic overflow of 5-HT. 15 references. (Author abstract modified)

168437 Yang, H.-Y. T.; Neff, N. H. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, St. Elizabeth's Hospital, Washington, DC 20032 **Beta-phenylethylamine: a specific substrate for type B monoamine oxidase of brain.** Journal of Pharmacology and Experimental Therapeutics. 187(2):365-371, 1973.

Beta-phenylethylamine and serotonin were oxidatively deaminated by separate forms of monoamine oxidase of rat brain when studied in vitro. These forms, designated as type A and type B enzyme, have different characteristics. For example, type A enzyme deaminated serotonin, was sensitive to the drug clorgyline, was resistant to the drug deprenyl and was heat stable. In contrast, type B enzyme deaminated beta-phenylethylamine, was resistant to clorgyline, was sensitive to deprenyl and was heat labile. Moreover, type A and type B enzyme activities could be partially separated by centrifugation of a continuous sucrose gradient. Beta-phenylethylamine and serotonin are present in mammalian brain. It was concluded that the amines of brain may be catabolized by specific types of monoamine oxidase in vivo. 30 references. (Author abstract)

168440 Ammon, H. P. T.; Orci, L.; Steinke, J. Department of Pharmacology, University of Erlangen, West Germany **Effect of chlorpromazine (CPZ) on insulin release in vivo and in vitro in the rat.** Journal of Pharmacology and Expeimental Therapeutics. 187(2):423-429, 1973.

The effect of chlorpromazine (CPZ) on glucose and insulin levels in the rat during a glucose tolerance test as well as on isolated pancreatic islets was investigated. Six rats in each of the treatment and controls groups were given CPZ intraperitoneally one hour before glucose tolerance testing at a dose of either 3.2or 32mg/kg. In isolated pancreatic rat islets, the effect of CPZ in concentrations between 0.001 and 1 mM on glucose induced insulin release and glucose oxidation was studied. It is concluded that CPZ exhibits its main action on the beta cell inhibiting glucose induced insulin release. Base line insulin levels are not decreased. Very high concentrations of CPZ decrease glucose oxidation in both the pentose phosphate shunt and the Embden-Meyerhof pathway. The paradoxical insulin release into the medium is the result of leakage due to cellular death. 37 references. (Author abstract modified)

168484 Zigmond, Michael J.; Stricker, Edward M. Psychobiology Program, Dept. of Biology, University of Pittsburgh, Pittsburgh, PA 15260 **Recovery of feeding and drinking by rats after intraventricular 6-hydroxydopamine or lateral hypothalamic lesions.** Science. 182(4113):717-720, 1973.

Details of the progressive recovery from aphagia and adipsia after intraventricular administration of 6-hydroxydopamine (6-HDA) were examined to determine if they are similar to the syndrome that is observed following electrolytic damage to the lateral hypothalamus. The rats were given intraventricular injections of 6-HDA after pretreatment with pargyline and became aphagic, adipsic and showed severe loss of brain

catecholamines. Like rats with lateral hypothalamic lesions, these animals gradually recover ingestive behaviors, although catecholamine depletions are permanent. Both groups decrease food and water intakes markedly after the administration of alpha-methyltyrosine at doses that do not affect the ingestive behavior of control animals. It is suggested that both the loss and recovery of feeding and drinking behaviors may involve central catecholamine containing neurons. 30 references. (Author abstract)

168485 Barker, Jeffery L.; Gainer, Harold. National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20014 **Pentobarbital: selective depression of excitatory postsynaptic potentials.** Science. 182(4113):720-722, 1973.

The depressive effects of pentobarbital (Nembutal) on synaptic transmission and postsynaptic potentials were studied by the use of several invertebrate preparations. Pentobarbital selectively and reversibly depressed both excitatory postsynaptic potentials and sodium dependent postsynaptic responses to putative excitatory transmitters without affecting either inhibitory postsynaptic potentials or chloride dependent and potassium dependent postsynaptic responses to putative transmitters. A selective depression of postsynaptic excitatory events was also observed with other central nervous system depressants (ethanol, chloroform, chloralose, diphenylhydantoin, and urethane). The results suggest that central and peripheral depression observed during general anesthesia is due to a selective depression of excitatory synaptic events. 20 references. (Author abstract)

168747 Paton, D. M. Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada **Effect of substituted tryptamines on the efflux of noradrenaline from adrenergic nerves in rabbit atria.** Journal of Pharmacy and Pharmacology (London). 25(11):905-907, 1973.

The effects of 5-hydroxytryptamine (5-HT) and of related substituted tryptamines on the efflux of (3H)(-) noradrenaline (3H-NA) from the cytosol of adrenergic nerves in rabbit atria were examined. All drugs were present from 60-90min. The compounds used were considerably less active than previously studied phenethylamines. Tryptamine was the most potent compound observed. Addition of a hydroxyl group to the indole ring reduced activity. Substitution of the 5-hydroxyl group in 5-HT with either a methyl or a methoxy group abolished activity, as did N-substitution with acetyl or ethyl groups. The results indicate that the structural requirements for indolethylamines to accelerate the efflux of 3H-NA are similar to those previously described for a series of phenethylamines, and support the growing evidence that a number of substituted tryptamines may influence the uptake, release, and efflux of noradrenaline from central and peripheral adrenergic neurons. 9 references.

168748 Fratta, W.; Biggio, G.; Mercuro, G.; Di Vittorio, P.; Tagliamonte, A.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Via Porcell 4, Cagliari, Italy **The effect of D- and L-p-chlorophenylalanine on the metabolism of 5-hydroxytryptamine in brain.** Journal of Pharmacy and Pharmacology (London). 25(11):908-909, 1973.

The possibility that the selective inhibition of p-chlorophenylalanine (PCPA) and 5-hydroxytryptamine (5-HT) originates from the incorporation of PCPA at an enzymatic site essential for their activity was investigated with male Wistar rats. Intraperitoneal injection of the isomers D-PCPA and L-PCPA were equally potent in producing a dose related depletion of brain 5-HT and 5-hydroxyindolacetic acid (5-HIAA). The increase in brain 5-HT level, normally observed after pargyline administration, was equally blocked in rats treated with D-PCPA or L-PCPA previously. The data indicate that both isomers act through a common mechanism in depleting brain 5-HT and 5-HIAA and in preventing the accumulation of 5-HT after pargyline. The inhibition of 5-HT synthesis by either isomer appears to be irreversible and dependent upon the slow formation of an active metabolite. 7 references.

168749 Izquierdo, Ivan; Tannhauser, Mario. Departmento de Fisiologia, Farmacologia e Biofisica, Instituto de Biociencias, U.F.R.G.S., Porto Alegre, RS, Brazil **The effect of cannabidiol on maximal electroshock seizures in rats.** Journal of Pharmacy and Pharmacology (London). 25(11):916-917, 1973.

The effect of varying doses of cannabidiol on maximal electroshock convulsions was studied with adult female albino rats. The 1 hr peak effect time found with a 3mg/kg-1 dose was chosen to study the effect of other doses. At 6mg/kb-1 and 12mg/kg-1 there was some protection against all components of the convulsion, and the ED50 for inhibition of the tonic extensor phase was 3mg/kg-

1. No alteration of stance and gait and no signs of ataxia were noted over 5 hours in rats treated with 12mg/kg-1 of cannabidiol. 11 references.

168750 Pollard, Helene; Bischoff, Serge; Schwartz, Jean-Charles. Unite de Neurobiologie (U.109), Centre I.N.S.E.R.M., 2 ter, rue d'Alesia, 75014 Paris, France **Decreased histamine synthesis in the rat brain by hypnotics and anaesthetics.** Journal of Pharmacy and Pharmacology (London). 25(11):920-922, 1973.

The effects of several hypnotics and anesthetics were investigated on the synthesis of (3H) histamine from labelled (3H)histidine administered intraventricularly to male Sprague-Dawley rats treated with sodium pentobarbitone, sodium phenobarbitone, chloral hydrate, or a mixture of oxygen and methoxyflurane. (3H)Histamine synthesis was decreased by 42 to 56% in the animals anesthetized during the 10 minute experimental period, except in those treated with methoxyflurane. There was a reduction up to 61% in (3H)methylhistamine in all groups. The results suggest that the turnover of the cerebral amine was reduced rapidly in anesthetized animals and indicate a possible dependence of brain histamine turnover on nerve impulse flow. 18 references.

168751 Modigh, K. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Effect of chlorimipramine on the rate of tryptophan hydroxylation in the intact and transected spinal cord.** Journal of Pharmacy and Pharmacology (London). 25(11):926-928, 1973.

The possible relation between retardation of the hydroxylation of tryptophan by chlorimipramine and changes in the nerve impulse flow was investigated by comparing the effect of chlorimipramine on the accumulation of 5-hydroxytryptophan (5-HTP) after decarboxylase inhibition, in the spinal cord of male Sprague-Dawley rats below and above an acute transection. Administered to unoperated animals, chlorimipramine significantly reduced 5-HTP accumulation in the brain and in the caudal part of the spinal cord but did not affect the accumulation of 5-HTP significantly in the cranial part of the spinal cord. Transection of the spinal cord caused a reduction of the 5-HTP accumulation in the spinal cord below the transection. Administered to transected animals, chlorimipramine reduced the 5-HTP accumulation in the cranial but not in the caudal part of the spinal cord. 22 references.

168817 Lauder, J.; Krebs, H.; Bloom, F. Laboratory of Neuropharmacology, St. Elizabeths Hospital, Washington, DC 20032 **Effects of p-chlorophenylalanine on differentiation of serotonergic receptive cells during embryogenesis. (Unpublished paper).** Washington, DC, NIMH, 1973. 1 p.

The timing of cell differentiation was studied in brain areas reported to receive inputs from the serotonin (5-HT) containing cells of the raphe nuclei in rats receiving p-chlorophenylalanine during gestation. In all the 5-HT target sites examined, an increase in the rate or amount of cell proliferation was indicated, and an increase in the number of cells differentiating on a given peak day as well as a delay and/or prolongation of cell differentiation by 1 to 2 days were observed as compared with controls and other non-5-HT target areas. Those areas previously reported to contain significant numbers of 5-HT terminals manifested the greatest changes. The results suggest that 5-HT may play a part in the regulation of cell proliferation and differentiation during embryogenesis in those neurons receiving 5-HT inputs in the adult. (Author abstract)

168839 Schubert, Johan. Farmakologiska Institutionen, Karolinska Institutet, S-10401 Stockholm 60, Sweden **Effect of chronic lithium treatment on monoamine metabolism in rat brain.** Psychopharmacologia (Berlin). 32(3):301-311, 1973.

The effect of chronic lithium (Li) treatment on monoamine metabolism in the rat brain was investigated. Lithium chloride was administered giving serum Li concentrations of about 0.4and 0.7meq/l. With the higher dose, accumulation of labeled 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in the brain during IV infusion of 3H-tryptopha (3H-TP) was increased. The effect was also present in the spinal cord following transection of 5-HT neurons, thus occurring independently of nerve impulse activity. The disappearance of labeled 5-HT from brain after IV injection of 3H-TP was reduced in Li treated animals indicating that Li diminishes release of 5-HT from its storage sites. Brain TP was augmented by Li, whereas levels of free and total TP in serum as well as its catabolism reflected by liver TP pyrrolase activity were unaltered. Accumulation and disappearance of labeled dopamine and noradrenaline formed from 14C-tyrosine in brain were not changed by Li treatment. It was concluded that chronic treatment of rats with Li within the low dose range

recommended for man affects 5-HT but not catecholamine synthesis and turnover in the brain. 10 references. (Author abstract modified)

168859 Almli, C. Robert. Department of Psychology, Ohio University, Athens, OH 45701 **/Presence of osmoreceptors for thirst in the lateral preoptic nucleus./** no title. Final Report, NIMH Grant, MH-22482. 1973. 6 p.

The possibility of the lateral preoptic nucleus (LPO) containing osmoreceptors for thirst was examined in rats. LPO units showed two types of response patterns to hypertonic sodium chloride injection. Type 1 units showed increased firing frequencies that were temporally coincident with onset of osmotically induced drinking, with high frequency responses maintained for the duration of the recording session. The type 2 units also showed such increased firing, but the high frequency response only lasted 2-3 min, and returned to baserate. Destruction of the LPO resulted in two distinct behavioral responses to osmotic stimuli. Large LPO lesions resulted in elongated latencies to drink and attenuated water intakes in response to various dipsogenic challenges. Smaller SPO lesions did not affect water intake; however, these rats also displayed elongated latencies to drink following dipsogenic challenges. Polyethylene glycol (PG) treatment was examined for possible cellular, in addition to extracellular, effects. Data suggest that PG may stimulate drinking through a cellular mechanism, and the osmoreceptors for thirst may reside within the LPO. (Author abstract modified)

168867 Costa, E.; Guidotti, A.; Zivkovic, B. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Short and long term regulation of tyrosine hydroxylase. (Unpublished paper).** Washington, DC, NIMH, 1973. 29 p.

Long-term and short-term regulation of tyrosine hydroxylase was studied in the dopaminergic terminals of the rat striatum and the chromaffin cells of the adrenal medulla, models exemplifying a form of immediate short-term control of the enzyme and a delayed long-term control of synthesis rate of tyrosine hydroxylase molecules, respectively. The various neuroleptics tested all increased tyrosine hydroxylase activity of striatal homogenates. The increase of tyrosine hydroxylase activity was localized only in the soluble fraction. The increase following administration of reserpine and methiothepin to different parts of the rat brain was located selectively in the catecholaminergic neurons of the striatum which are mostly dopaminergic. The results suggest that neuroleptics which increase the firing rates of dopaminergic neurons change the affinity of the enzyme for DMPH4 and that the adenylate cyclase in adrenal medulla can be regulated by the degree of stimulation of nicotinic receptors. 44 references.

168869 Neff, Norton H.; Yang, Hsiu-Ying T.; Fuentes, Jose A. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The use of selective MAO inhibitor drugs to modify amine metabolism in brain. (Unpublished paper).** Washington, DC, NIMH, 1973. 9 p.

Some of the characteristics of monoamine oxidase (MAO) inhibitor drugs are discussed based primarily upon rat studies. Multiple forms of MAO are present in the brain and may be separate or single proteins, deaminate separate substrates as well as some of the same substrates, can be separated partially by density gradient centrifugation, and can be inhibited differentially with drugs. The specific inhibitor drugs may be useful tools for studying the functional role of the brain amines, and knowledge of their specific traits and properties will probably alter the treatment of many disorders ascribed to abnormal amine metabolism. 15 references.

169067 Burstein, Sumner. Worchester Foundation for Experimental Biology, Shrewsbury, MA **Prostaglandins and cannabis: a possible mode of action for THC.** Psychopharmacology Bulletin. 9(4):25-26, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, an examination of the effects of delta1-tetrahydrocannabinol (THC) and several other cannabinoids on the prostaglandin EL (PGE) synthetase activity of seminal vesicle microsomes was discussed. It was demonstrated that many of the natural cannabinoids can inhibit PG synthesis in vitro. This could provide a basis for explaining the psychoactive properties of delta1-THC and delta6-THC and in addition might explain some of the other pharmacological actions of the cannabinoids. 10 references. (Journal abstract modified)

169071 Overton, Donald A. Dept. of Psychiatry, Temple Medical Center, Eastern Pennsylvania

Psychiatric Institute, Philadelphia, PA **State dependent learning produced by addicting drugs.** Psychopharmacology Bulletin. 9(4):29-31, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the discriminability of several abused and nonabused drugs were evaluated in order to establish a background for the determination of the correlation between abuse potential and state dependent learning. The data suggest a rough correlation between discriminability and abuse potential, but there are exceptions. Some relatively nonabused drugs, such as Librium and antimuscarinics, do have high discriminability. Conversely, caffeing is nondiscriminable although it could be classified as an abused drug. It is suggested that if a method can be developed for similarly quantifying the abuse potential of various drugs, then the apparent correlation between abuse potential and state dependent learning can also be more quantitatively evaluated. (Journal abstract modified)

169120 Tarsy, Daniel; Baldessarini, Ross J. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Pharmacologically induced behavioural supersensitivity to apomorphine.** Nature New Biology (London). 245(148):262-263, 1973.

A study to determine whether chronic pretreatment with an antiadrenergic drug, apomorphine, would enhance a stereotyped response believed to be mediated by dopamine is reported. Apomorphine was used on young male rats because it is believed to have a direct action on dopamine receptors in the striatum. Prolonged administration of a neuroleptic drug can lead to persistent and irreversible dyskinesias which often appear or worsen on withdrawal of the drug. Denervation supersensitivity to dopamine, secondary to prolonged blockade of dopamine receptors in the striatum, has been proposed as a possible mechanism for the phenomenon. Results support the concept that prolonged exposure to drugs which interfere with neurotransmission by either pre or postsynaptic mechanisms can increase sensitivity to subsequent stimulation of the postsynaptic receptors in the brain. 24 references.

169467 Izquierdo, J. A.; Baratti, C. M.; Torrelio, M.; Arevalo, L.; McGaugh, J. L. Catedra de Farmacologia Experimental, Facultad de Farmacia y Bioquimica, Junin 956, Buenos Aires, Argentina **Effects of food deprivation, discrimination experience and physostigmine on choline acetylase and acetylcholine esterase in the dorsal hippocampus and frontal cortex of rats.** Psychopharmacologia (Berlin). 33(1):103-110, 1973.

The effects of food deprivation and preliminary training treatments on choline acetylase and acetylcholine esterase activity in the dorsal hippocampus and frontal cortex of rats have been investigated. In addition, blood sugar and adrenal epinephrine levels were examined. The activity of choline acetylase and the levels of blood sugar and adrenal epinephrine were significantly altered during various stages of preliminary training but all values were comparable to preexperimental levels before discrimination commenced. In addition, rats were injected physostigmine salicylate or saline i.p. each day immediately after receiving three training trials on a food motivated black - white task. The physostigmine injected rats were significantly better than the controls in rate learning. No differences were observed in choline acetylase activity in the dorsal hippocampus and frontal cortex in discriminating rats treated with physostigmine or saline. However, choline acetylase activity is lower in treated and control rats which did not discriminate at the end of the fourteenth session. 20 references. (Author abstract)

169471 Mazurkiewicz-Kwilecki, I. M.; Filczewski, M. Department of Pharmacology, University of Ottawa, Ottawa, Ontario, Canada KIN 6N5 **The effects of chronic treatment with delta9-tetrahydrocannabinol on catecholamine synthesis in the rat.** Psychopharmacologia (Berlin). 33(1):71-79, 1973.

The effects of chronic treatment with delta9-tetrahydrocannabinol (THC) on catecholamine synthesis were studied in the rat. Chronic administration of THC to rats resulted in a significant increase in the synthesis of H3-catecholamines in the brain and adrenals. Endogenous noradrenaline and dopamine concentration in the brain, adrenaline and noradrenaline level in adrenals and cardiac noradrenaline content of experimental rats did not differ from those of control animals injected with the solvent alone. 34 references. (Author abstract)

169472 Karniol, I. G.; Carlini, E. A. Department of Psychobiology, Escola Paulista de Medicina, Sao Paulo, Brazil **Pharmacological interaction between cannabidiol and delta9-tetrahydrocannabinol.** Psychopharmacologia (Berlin). 33(1):53-70, 1973.

The pharmacological interaction between cannabidiol (CBD) and (-)delta9-trans-tetrahydrocannabinol (THC) was studied in rabbits, mice and rats by administering mixtures containing varying amounts of both substances. CBD blocked the following effects of THC: catatonia in mice, corneal areflexia in rabbits, the increased defecation and decreased ambulation after chronic treatment and exposures of rats in an open field arena, and the aggressiveness of rats previously stressed by REM sleep deprivation. CBD potentiated the THC induced analgesia in mice and the THC impairing effect on climbing rope performance of rats. These interactions are tentatively explained by postulating that CBD directly antagonizes the excitatory effects and/or indirectly potentiates the depressant effects of THC. 41 references. (Author abstract)

169474 Blasig, J.; Herz, A.; Reinhold, K.; Zieglgansberger, S. Max-Planck-Institut fur Psychiatrie, 8000 Munchen 40, Kraepelinstrasse 2, Germany **Development of physical dependence on morphine in respect to time and dosage and quantification of the precipitated withdrawal syndrome in rats.** Psychopharmacologia (Berlin). 33(1):19-38, 1973.

The development of physical dependence on morphine was studied with respect to time and dosage. In withdrawal the intensity of recessive signs like writhing and wet dog shaking declined when dominant signs like jumping, flying (a vigorous kind of jumping) and teeth chattering increased. An inverse relationship between the occurrence of various signs was shown within the 30 min observation period. In another experiment in which the interval between each morphine implantation was prolonged the frequency of some signs like jumping and teeth chattering tended to plateau. This finding was correlated to some kind of steady state on resorption of morphine from the subcutaneous depots, as was found in chemical analysis. 22 references. (Author abstract modified)

169675 Liu, R. K.; Walford, R. L. Department of Pathology, UCLA School of Medicine, Los Angeles, CA 90024 **The effect of lowered body temperature on lifespan and immune and non-immune processes.** Gerontologia (Basel). 18(5-6):363-388, 1972.

The effect of lowered body temperature on lifespan and immune and nonimmune processes in invertebrates and vertebrates is reviewed. It is suggested that decreasing the environmental temperature tends to increase lifespan of invertebrates and polkilothermic vertebrates. Thermolabile homeotherms appear to live longer than comparably sized species which do not undergo periodic, natural lowering of their body temperatures. Findings indicate that even a mild lowering of temperature suppresses both humoral and cellular immune processes in polkilotherms. Initial studies aimed at inducing mild, chronic or intermittent hypothermia in mice with chlorpromazine and marihuana derivatives are described. 133 references. (Author abstract modified)

169689 Scholes, N. W. Creighton University School of Medicine, Department of Physiology-Pharmacology, Omaha, NB 68178 **Lysergic acid diethylamide (LSD-25) and gamma amino butyric acid (GABA) interaction on spontaneous potentials and the evoked response in the avian tectum.** Proceedings of the Society for Experimental Biology and Medicine. 144(2):623-625, 1973.

The action of the neuroamine gamma aminobutyric acid (GABA) on the effects of LSD in baby chicks is reported. The young avian tectum preparation was considered to be a suitable tool for the study of antagonists to psychotoxic drugs. Experimental animals were 19 acutely prepared New Hampshire chicks of 1 or 2 weeks of age. GABA and LSD-25 were individually administered by slow infusion. It was discovered that the parenteral administration of GABA causes an inhibition of the photically evoked response recorded in the tectum. GABA acts primarily as an inhibitor upon axosomatic synapses. The action of LSD on the electrophysiology of the tectum is discussed. It is suggested that the central mechanism of action of all hallucinogens may involve the GABA system in the sensory areas of the CNS. 15 references.

169782 Blum, K.; Calhoun, W.; Merritt, J.; Wallace, J. E. Department of Pharmacology, University of Texas Health Science Center at San Antonio, San Antonio, TX **L-DOPA: effect on ethanol narcosis and brain biogenic amines in mice.** Nature (London). 242(5397):407-409, 1973.

Further evidence is presented to implicate dopamine in L-DOPA induced augmentation of ethanol narcosis in mice, and the effects of L-DOPA on brain biogenic amines was investigated. Results indicate that L-DOPA induced enhancement of ethanol sleep noted in Swiss-Webster mice was due to the rise in brain dopamine (DA).

L-DOPA is converted by a pyridoxal phosphate dependent decarboxylation reaction to dopamine and reacts with pyridoxal phosphate in vitro. Removal of pyridoxal phosphate by chronic L-DOPA possibly lessened decarboxylase activity with a decreased conversion of DOPA to DA. Diminished formation of DA, however, may be due to decreased brain L-DOPA uptake. 15 references.

170072 Buchar, E.; Masek, K.; Obermajerova, H.; Seifert, J.; Havlik, I. Institute of Pharmacology, Czechoslovak Academy of Sciences, Albertov 4, 128 00 Prague 2, Czechoslovakia **Lipid-induced changes of pentobarbital distribution and metabolism.** Pharmacology (Basel). 10(3):152-160, 1973.

The mechanism by which a perorally administered lipid compound, palmitoylethanolamide (PEA), potentiates the hypnotic effect of pentobarbital and the role of liver microsomal fatty acids in pentobarbital distribution and metabolism were studied. The feeding of PEA to mice for 12 days resulted in a marked prolongation of pentobarbital hypnosis. Analysis of 14C-pentobarbital levels in blood and tissues of PEA treated animals has shown a lower level of radioactivity in blood and higher activity in tissues after 15 minutes, which indicates that PEA influences the blood/tissue distribution of barbiturate. Determination of 14C-pentobarbital metabolites has revealed that the metabolism of pentobarbital in liver is decreased. The prolongation of pentobarbital hypnosis in PEA treated mice may be explained on the basis of higher levels of pentobarbital in brain. Microsomal fatty acid analysis in PEA treated mice demonstrated a marked change in the composition of fatty acids which suggests that there may be a relationship between microsomal fatty acid composition and drug metabolism. 27 references. (Journal abstract modified)

170073 Kilian, Marion; Frey, H.-H. Department of Pharmacology and Toxicology, School of Veterinary Medicine, Free University, Berlin, Germany **Thresholds for electro- and chemoconvulsions in mice after termination of treatment with phenobarbital.** Pharmacology (Basel). 10(3):169-177, 1973.

The thresholds for electroconvulsions and pentetrazole convulsions in mice after termination of treatment with doses of phenobarbital which were so chosen as to permit the construction of an anticonvulsant dose effect relationship in the maximum electroshock seizure test and in the pentetrazole seizure threshold test were examined. The thresholds for electroconvulsion or the clonic and tonic components of the pentetrazole convulsion were determined immediately after withdrawal of phenobarbital and 24, 48, and 72 hours later. The electroconvulsive threshold fell to values significantly lower than the threshold in untreated controls at 24 hours, but had recovered to control values after 48 hours. The pentetrazole thresholds, too, showed a highly significant decrease below the control values at 24 hours, but even after 48 and 72 hours, they were significantly lowered in some instances. The coincidence of hyperexcitability and weight loss points to the development of physical dependence to the drug. 18 references. (Journal abstract modified)

170082 Axelrod, Julius. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Biochemical and pharmacological approaches in the study of sympathetic nerves. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 39 p.

Work using biochemical and pharmacological approaches in studying sympathetic nerves is reviewed, stressing efforts related to the biochemistry of the adrenergic nervous system. These research attempts included: studies of the metabolism of analgesics, anticoagulants, adrenergic blocking agents and caffeine; the biotransformation of phenylethylamine derivatives; the metabolism and physiological disposition of LSD and the enzymes involved in the metabolic action of narcotic drugs; the metabolism of adrenaline, specifically isolation of the methyltransferase enzymes for use in searching for new biogenic amines in the nervous system and in devising sensitive assays to measure noradrenaline, dopamine, and serotonin, as well as in elucidating the metabolic pathways for catecholamines; the uptake and storage of radioactive noradrenaline in sympathetic nerves; the labelling of brain noradrenergic neurons and the regulatory mechanisms for adrenaline formation, and pineal research. 72 references.

170083 Sack, Robert L.; Goodwin, Frederick K. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Selective inhibition of norepinephrine synthesis in manic-depressive patients with a dopamine-beta-hydroxylase inhibitor. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 15 p.

Fusaric acid, as an inhibitor of dopamine-beta-hydroxylase (DBH), was administered to manic and depressed patients as an approach for testing the CA (central amine) hypothesis of affective disorder. The hypothesis states that depression is associated with a functional deficit of norepinephrine (NE) at critical synapses in the central nervous system, and that mania is associated with a functional excess of NE. It is based on observations of the clinical effects of drugs known to alter CA function in animals. No clinical benefit was observed, despite significant effects on central amine metabolism. The findings are most easily explained by hypothesizing a dopamine, rather than a NE, excess in mania. 44 references. (Author abstract modified)

170086 Guidotti, A.; Zivkovic, B.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Possible involvement of cyclic nucleotides in the stimulation of pituitary function elicited by reserpine. (Unpublished paper).** Washington, DC, NIMH, 1973. 8 p.

The activation of pituitary adrenal axis by reserpine was studied to determine whether or not it is related to monoaminergic neuronal function in rats. Pituitary adenosine 3',5'-monophosphate (cAMP) and plasma corticosteroids were measured after administration of drugs which change the function of monoaminergic neurons. Pargyline, 15mg/kg i.v.,prevents the reserpine induced changes of pituitary cAMP and plasma corticosteroids. Deprenyl (5mg/kg i.v.), a monoamine oxidase inhibitor specific for dopamine, and parachlorophenylalanine do not prevent changes induced by reserpine. Results support the concept that norepinephrine, and not dopamine or serotonin, express a negative control on the hypothalamus pituitary adrenal function. 20 references. (Author abstract modified)

170163 Haavik, Coryce O.; Hardman, Harold F. Department of Pharmacology, Medical College of Wisconsin, 561 N. Fifteenth St., Milwaukee, WI 53233 **Evaluation of the hypothermic action of tetrahydrocannabinols in mice and squirrel monkeys.** Journal of Pharmacology and Experimental Therapeutics. 187(3):568-574, 1973.

The hypothermic action of delta9-tetrahydrocannabinol (delta9-THC), 11-hydroxy-delta8-tetrahydrocannabinol (11-OH-delta8-THC) and the synthetic tetrahydrocannabinol, 1-hydroxy-3-(1,2-dimethylheptyl)-6,6,9- trimethyl-7,8,9,10-tetrahydro-6-dibenzopyran (DMHP) were studied in mice and squirrel monkeys. Studies carried out at 20 deg C, where toxicity is minimal and hypothermia to delta9-THC is nearly maximal, a dose response relationship was shown for the hypothermic response to intravenous delta9-THC, 11-OH-delta8-THC and DMHP in the mouse. Maximal hypothermia recorded was 12.77 degrees C (delta9-THC, 32mg/kg), greater than 12.45 degrees C (DMHP, 2mg/kg) and 6.20 degrees C (11-OH-delta8-THC, 32mg/kg). Hypothermic responses of comparable magnitude to mice but slower in onset were recorded in the monkey after intravenous administration of delta9-THC or DMHP at an ambient temperature of 24 deg C. The importance of ambient temperature control during studies of the action of tetrahydrocannabinols on other systems is discussed. 17 references. (Author abstract modified)

170747 Koslow, S. H.; Bjegovic, M.; Lofstrandh, S. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Simultaneous mass fragmentographic assay of norepinephrine (NE), epinephrine (E) and dopamine (DA) in rat sympathetic ganglion: effects of dexamethasone in new born and adult rats. (Unpublished paper).** Washington, DC, NIMH, 1973. 1 p.

The effects of administration of dexamethasone, a glucocorticoid, on norepinephrine (NE), epinephrine (E), and dopamine (DA) on newborn and adult rat sympathetic ganglion are investigated. The effects of dexamethasone on the catecholamine content were investigated using mass fragmentography. After 8 days of dexamethasone treatment, there is a significant increase in concentration of the catecholamines which is apparently restricted to the cell bodies, since there is no increase in the catecholamine content of the pineal gland or the salivary gland. Both tissues receive innervation from the superior cervical ganglion (SCG). In adult Ss, dexamethasone failed to alter the catecholamine content of the SCG. Is is concluded that although there is a possibility that the effect of dexamethasone is on preexisting ganglion cell bodies, the absence of a change in the catecholamine content of the pineal and salivary glands and of adult SCG after dexamethasone suggests that the action is on undifferentiated stem cells. (Author abstract modified)

170748 Suria, Amin Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Diazepam and post-tetanic potentiation: possible role of prostaglandins. (Unpublished paper).** Washington, DC, NIMH, 1973. 1 p.

Posttetanic potentiation (PTP) of the fast excitatory postsynaptic potential (EPSP) in the curarized sympathetic ganglion of the bullfrog was studied and found inhibited by diazepam in a reproducible, dose - dependent manner. Prostaglandins (PGs) of the E series mimicked the action of diazepam, also in a dose - dependent fashion, and arachidonic acid inhibited the PTP of EPSP as well. The inhibition obtained with diazepam could be potentiated in the presence of PGs or arachidonic acid. Pretreating the ganglion with 5,8,11,14-eicosatetraynoic acid, a prostaglandin synthetase blocker, abolished diazepam and arachidonic acid inhibition of PTP but not that of PGs. If the receptors for prostaglandins were blocked with a dibenzoxazepine derivative, the response to diazepam, arachidonic acid, as well as to PGs, was abolished. None of these compounds inhibited the potential evoked by single shock. Data indicate that PGs may be involved in the regulation of PTP. The frequency and duration of the conditioning train required to elicit maximal PTP was reduced in the presence of SC 19220 of ETA. Findings further suggest the inhibition of PTP of EPSP by diazepam may be mediated by PGs. (Author abstract modified)

170755 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, St. Elizabeths Hospital, Washington, DC 20032 **Specific activation of striatal tyrosine hydroxylase (TH) by neuroleptics. (Unpublished paper).** Washington, DC, NIMH, 1973. 1 p.

A single, intraperitoneal injection of haloperidol, methiothepin, pimozide, and reserpine increases tyrosine hydroxylase (TH) activity of striatal homogenates, but not that of hypothalamus, brain stem or adrenal gland. The maximum increase occurs in 30 min after methiothepin, 1 hr after haloperidol or pimozide, and 2 hrs after reserpine. The TH increase obtained with neuroleptics lasts for 12 hrs, whereas that from reserpine lasts longer than 24 hrs. Neuroleptics increase only the soluble TH activity of homogenates; particle-bound TH activity remains unchanged. During the increase of activity elicited by neuroleptics and reserpine the Vmax for tyrosine is doubled, while its Km is unchanged. Amphetamine, morphine, neuroleptics, and reserpine increase the dopamine turnover rate in vivo. However, only reserpine and neuroleptics increase striatal TH. It is concluded that since the neuroleptic, but not amphetamine and morphine, increase the pulse flow in nigro striatal neurons, rates of neuronal activity may regulate TH by decreasing the Km for DMPH4 and 6MPH4. (Author abstract modified)

170837 Schwartz, Morton A.; Postma, Edward; Kolis, Stanley J.; Leon, Arthur S. Department of Biochemistry and Drug Metabolism, Hoffman-La Roche, Inc., Nutley, NJ 07110 **Metabolites of Bromazepam, a benzodiazepine, in the human, dog, rat, and mouse.** Journal of Pharmaceutical Sciences. 62(11):1776-1779, 1973.

The biotransformation of bromazepam, 7-bromo-1,3-dihydro-5-(2-pyridyl)-2H-1,4-benzodiazepin-2-one, was studied in four species. Four metabolites were identified and their excretion was quantitatively determined. The major urinary metabolites excreted by three women given single 12mg. oral doses of bromazepam-5-14C were the conjugated forms of 3-hydroxybromazepam (I), accounting for 13-30% of the dose, and 2-(2-amino-5-bromo-3-hydroxybenzoyl)pyridine (IV), accounting for 4-25% of the dose. Conjugated I was also the major metabolite in three dogs and four groups of mice administered 14C-bromazepam, but its excretion by four rats was very limited. Together with I, metabolite IV and 2-(2-amino-5-bromobenzoyl)pyridine were detected in the excreta of the human, dog, rat, and mouse. Although the pyridyl N-oxide derivative of bromazepam was not detected as a metabolite in any species, the N-oxide was a minor metabolite in dog urine. This is the first reported instance of metabolic N4-oxidation of a 1,4-benzodiazepin-2-one. 11 references. (Journal abstract)

170874 Bell, J. A.; Martin, W. R. NIDA Addiction Research Center, P.O. Box 2000 Lexington, KY 40507 **The effect of L-tryptophan (TP) on cutaneous C-fiber (CFR) and polysynaptic (PSR) reflexes in acute decerebrate spinal cats and the effect of pretreatment with para-chlorophenylalanine (pCPA) on the action of TP. (Unpublished paper).** Lexington, KY, NIMH 1973. 1 p.

The action of serotonin (5HT) on cutaneous C-fiber (CFR) in cats was assessed and compared with the action of tryptamine (T). CFR and polysynaptic reflexes (PSR) were evoked by

stimulation of the superficial peroneal nerve of the acute decerebrate spinal cat and recorded from an ipsilateral ventral root. L-tryptophan (TP) administration increases serotonin selectively in serotonin containing neurons. Facilitation was antagonized by cyproheptadine. In cats pretreated with 2 injections of para-chlorophenylalanine (pCPA) methyl ester 24 hr apart, TP increased the CFR over 200% of control at 60 min. If in pCPA pretreated cats, TP is preferentially metabolized to T as it is in the rat, facilitation of CFR by TP in the pCPA treated cat is correlated with an increase in spinal cord T. In the normal cat, facilitation of CFR by TP is correlated with an increase in spinal cord 5HT. (Author abstract modified)

170876 Hanbauer, I.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH Bethesda, MD 20014 **Tyrosine hydroxylase (TH) activity and cyclic 3,5-adenosine monophosphate (cAMP) concentrations in sympathetic ganglia of rats: effects of drugs acting at cholinergic and adrenergic synapses. (Unpublished paper).** Washington, DC, NIMH, 1973. 1 p.

Repeated injections of isoproterenol (ISOP) increase tyrosine hydroxylase (TH) in intact superior cervical sympathetic ganglia after 48 hours in rats. One of two doses of ISOP fails to increase TH. The affinity constants of TH are unaltered when TH is increased by ISOP. Four injections of ISOP also increase TH in decentralized ganglia. Pretreatment with propranolol or practolol prevents the action of ISOP, whereas one or three injections of the beta blockers following the last ISOP injection fail to block TH increase. Epinephrine, but not equimolar doses of norepinephrine, followed 15 min. later by phenoxybenzamine increases TH. Carbamylcholine, atropine, hexamethonium, and amphetamine fail to increase TH activity. ISOP promptly increases cyclic (cAMP) concentrations in ganglia for about 40 min. After three or four injections of ISOP, ganglionic cAMP is increased for about 2 hrs. It is suggested that a beta-adrenergic receptor located in ganglia can regulate cAMP concentrations in the TH activity. (Author abstract modified)

171305 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Yorkshire, England **Is there a relationship between the involvement of extrapyramidal and mesolimbic brain areas with the cataleptic action of neuroleptic agents and their clinical antipsychotic effect?** Psychopharmacologia (Berlin). 32(2):161-170, 1973.

The electrolytic brain lesion technique was used in the rat to disrupt the ascending dopaminergic pathways to the extrapyramidal (striatal) and mesolimbic brain areas in the lateral hypothalamus and the pathways to the mesolimbic brain areas only in the rostral Kypothalamus. The cataleptic effects of the neuroleptic agents spiroperidol and perphenazine were enhanced in the acute stage following the lateral hypothalamic lesions but were unmodified or reduced by rostral hypothalamic lesions. Both lateral and rostral hypothalamic lesions markedly reduced or abolished the cataleptic ability of all neuroleptics tested in the chronic stage. The cataleptic activities of the nonneuroleptic agents metoclopramide and bulbocapnine were unmodified or potentiated by lesions in the lateral hypothalamus and potentiated or unmodified by lesions in the rostral hypothalamus respectively during the acute stage. In the chronic stage the cataleptic effects of both agents were markedly reduced or abolished in animals with lateral or rostral hypothalamic lesions. 21 references. (Author abstract)

171307 Hackmann, Eva; Wirz-Justice, Anna; Lichtsteiner, M. Biochemisches Laboratorium der Psychiatrischen Universitatsklinik, 4056 Basel, Switzerland **The uptake of dopamine and serotonin in rat brain during progesterone decline.** Psychopharmacologia (Berlin). 32(2):183-191, 1973.

A possible relevant animal model for the hormone triggered emotional disturbances of premenstruum, postpartum, and the menopause was investigated. The common characteristic situation of progesterone decline was simulated in ovariectomized rats, studied 12, 24, 36, and 48 h after the last of a week long 12 hourly series of progesterone injections. In vitro uptake of 3H-dopamine and 3H-serotonin in slices from cortex, preoptic hypothalamus, thalamus, midbrain and striatum was measured. Serotonin uptake was reduced in progesterone treated slices from the preoptic hypothalamus 24 h, from the thalamus 36 h after the last injection, whereas no change in dopamine uptake in any region was noted. Dopamine uptake was found to increase with time after the last injection (a possible effect of the particular stress situation of chronic injection), and was also significantly higher at 8 h than at 20 h in cortex, midbrain, and striatum. Serotonin uptake did not vary with the time of day. 27 references. (Author abstract)

171600 Aquilonius, S.-M.; Flentge, F.; Schuberth, J.; Sparf, B.; Sundwall, A. Department of Neurology, University Hospital of Uppsala, S-750 14 Uppsala, Sweden **Synthesis of acetylcholine in brain nerve terminals during consciousness and barbiturate anaesthesia.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):1, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the synthesis of acetylcholine (ACh) in brain nerve terminals during consciousness and barbiturate anesthesia was reported. After intravenous injection of choline (Cn) in mice, a fraction containing nerve terminals was isolated from a brain sucrose homogenate. In vitro characteristics and electron microscopy indicate that these fractions represent isolated synaptic vesicles and cytoplasm. Maximal incorporation in labelled ACh during consciousness was found at the shortest time intervals studied, 0.25-0.5min. Specific radioactivity of ACh was significantly higher in the vesicular fraction in the time interval 0.25-9 min and about the same in the two fractions 15 min after 3H-Ch injection. Barbiturate anesthesia preferentially decreased incorporation of labelled ACh in the vesicular fraction. It is suggested that an important site of ACh synthesis is closely associated to the synaptic vesicle and that barbiturate anesthesia is accompanied by reduced ACh synthesis in this functionally important ACh pool. (Author abstract modified)

171601 Ekwall, T.; Wahlstrom, G. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Tolerance to hexobarbital and supersensitivity to pilocarpine induced by chronic barbital treatment in the rat.** Acta Pharmacologia et Toxicologica (Kobenhavn). 31(Supplement 1):2, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, an evaluation of denervation supersensitivity in tolerance to barbiturates is reported. The temperature depressing effect of pilocarpine was compared with a threshold dose of hexobarbital after chronic barbital treatment. The changes in threshold and in temperature followed each other. There was a large increase in threshold after the end of the treatment accompanied by a decrease in temperature. After three weeks there was a new increase in threshold which also was accompanied by a new decrease in temperature. It is concluded that denervation supersensitivity in the cholinergic part of the central nervous system could be involved in the tolerance to barbiturates. (Author abstract modified)

171602 Lewander, T. Psychiatric Research Center, Ulleraker Hospital, University of Uppsala, S-75017 Uppsala, Sweden **Tolerance and cross-tolerance to the anorexigenic effect of some amphetamine derivatives in rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):3, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, tolerance and cross-tolerance to the anorexigenic effects of dl-amphetamine, d-amphetamine and l-amphetamine, phenmetrazine, p-chloramphetamine and fenfluramine are reported. After 1-2 days on the respective drugs, except p-chloroamphetamine, tolerance to the anorexigenic effect began to develop and after approximately 10 days maximal tolerance about 75% of the control animals' food intake, was reached. Tolerance to p-chloroamphetamine was already evident after the third injection and was almost complete after 5 days. In rats tolerant to dl-amphetamine, d-amphetamine, and l-amphetamine and phenmetrazine the duration of the anorexigenic effect was reduced, while in p-chloroamphetamine and fenfluramine tolerant rats the intensity of the effect was weakened. Rats made tolerant to l-amphetamine and phenmetrazine were cross-tolerant towards d-amphetamine. Rats tolerant to d-amphetamine, phenmetrazine and p-chloroamphetamine were cross-tolerant towards fenfluramine. It is concluded that the different drugs, partly at least, share similar mechanisms of action with regard to the anorexigenic effect. 1 reference. (Author abstract modified)

171604 Lidbrink, P. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Turnover-changes in central monoamine neuron systems after minor tranquillizers and barbiturates.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):5, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effect of minor tranquillizers of the benzodiazepine group and barbiturates on turnover of central monoamines in the rat was reported. Chlordiazepoxide, diazepam and phenobarbitone decreased the turnover of noradrenaline (NA) in NA nerve terminals of the cerebral cortex, whereas no effect was observed in the hypothalamus. These drugs counteracted

the stress induced increase in NA turnover in both areas. The dopamine (DA) nerve terminals of the neostriatum showed a decreased turnover. Stress alone also reduced the turnover of striatal DA. The doses used induced sedation and hypnosis. Lower doses caused no change in turnover and had little effect on the gross behavior of the animals. The effects were shown not to be related to interference with the uptake, retention of field stimulated release in vitro, inhibition of monoamine oxidase in the brain regions studied or receptor stimulation. This suggests that the effects are indirect, the input to the various monoamine neuron systems having different sensitivity to these drugs. (Author abstract modified)

171605 Jonsson, G.; Fuxe, K. Department of Histology, Karolinska Institutet S-104 01 Stockholm, Sweden **Effect of tetrahydrocannabinols on central monoamine neurons.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):6, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effect of delta9-tetrahydrocannabinol (THC) on uptake - storage mechanisms and amine turnover in monoamine containing neurons in the central nervous system of the rat were reported. In vivo administration of THC caused an increase in uptake of 3H-noradrenaline (NA), 3H-dopamine (DA) and 3H-5-hydroxytryptamine (5-HT) into NA, DA and 5-HT neurons whereas no effects on the retention of 3H-amine were observed. Administration of THC in vitro did not produce any effects on the uptake and storage of 3H-amine. THC also caused an increase in NA and 5-HT turnover, whereas the DA turnover was decreased. The present results indicate that THC or metabolites of this compound might produce changes in the membrane properties of the axonal membrane of central monoamine neurons. The functional significance of the THC induced changes in monoamine turnover were discussed. (Author abstract modified)

171606 Aquilonius, S.-M.; Lundholm, B.; Winbladh, B. Department of Neurology, Akad. Sjukhuset, Uppsala, Sweden **Interaction between atropine and oxotremorine on cortical acetylcholine and motor activity.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):7, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the hypothesis that cortical sites are responsible for the effect of antimuscarinic drugs on acetylcholine release (AchR) while subcortical sites are involved in the effects on motor activity (MA) was examined. The muscarinic drug oxotremorine given simultaneously or 30 minutes before atropine inhibited the atropine induced increase in MA about 75%. However, regarding the AChR there was no antidote effect of oxotremorine, when given as above before atropine. With a time interval of 8 minutes between the drugs, a slight reduction of the enhancement of AChR was obtained during 1 hour. It is concluded that oxotremorine counteracts the effects of atropine more efficiently regarding the subcortically produced MA than the cortical AChR. The findings that oxotremorine increases the ACh content in the basal ganglia more than in whole brain also suggest a mainly subcortical action of the drug. 3 references. (Author abstract modified)

171610 Schulz, R.; Frey, H.-H. Department of Pharmacology and Toxicology, School of Veterinary Medicine, Free University, Koserstrasse 20, D-1 Berlin 33, Germany **Study into the mechanism of the anorectic action of amphetamine and its p-chloro analogue.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):12, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the mechanism of the anorectic action of amphetamine and its p-chloro analogue was reported. The hypothesis of a tryptaminergic mediation of drug-induced anorexia was tested in male rats. d-Amphetamine and d-p-Cl-amphetamine were applied anorectic agents. The effect of an ED 95 was strongly antagonized by pretreatment with p-Chlorophenylalanine. Cyproheptadine displayed a dose dependent antagonism to amphetamine in the dose range of 0.4-1.6mg/kg but only a weak one to p-Cl-amphetamine in a dose of 0.4mg/kg. Both amphetamines were shown to enhance the turnover of 5-HT in the hypothalamus. The anorectic effect could also be antagonized by manipulations of the central catecholamines. The results point to a role of both 5-hydroxytryptamine and catecholamines in the mediation of drug-induced anorexia, however, the role of 5-HT seems to be of greater importance in the case of p-Cl-amphetamine, that of the catecholamines in the case of amphetamine. (Author abstract modified)

171613 Airaksinen, M. M.; Castren, O.; Fristrom, S.; Saarikoski, S. Pharmacological Division of the Department of Pharmacy, University of Helsinki, Helsinki, Finland **The effects of 6-OH-**

dopamine on the reproduction and NA and 5HT contents of some tissues in mice. Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):18, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of 6-OH-dopamine (6HD) on the reproduction and noradrenaline (NA) and 5-hydroxytryptamine (5-HT) contents of some tissues in mice were reported. No significant effect on the estrus cycle was noted and when put together with males the animals became pregnant normally. The litter size of the treated mice, however, was significantly smaller than that of the controls. NA disappeared nearly totally from the iris and tubae. The contents of NA (but not of 5HT) were decreased to about 30% in heart and kidneys and to about 70% in brain. The NA contents of the total fetuses and in heart and brain of the newborn rats was also dropped from that of control fetuses and newborns. It is concluded that 6HD goes through the placenta and may act on the fetus. (Author abstract modified)

171622 Anden, N. -E.; Magnusson, T. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Influences of drugs on the increases in brain dopamine produced by axotomy of gammahydroxybutyric acid (GHBA).** Acta Pharmacologica et Toxicologica (Kobenhavn). 31 (Supplement 1):27, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the influences of drugs on the increases in brain dopamine produced by axotomy or gammahydroxybutyric acid (GHBA) were reported. Dexamphetamine sulphate completely prevented the rise in brain dopamine before the operation or the GHBA administration. When given 30 minutes after, instead of before, dexamphetamine partially prevented the increases. Apomorphine produced a slight suppression of the dopamine rise, especially after hemisection. Haloperidol did not induce any significant change in the increases. Nor did it influence the effect of amphetamine when given 30 minutes before this drug. The reduction of brain dopamine induced by alpha-methyltyrosine methylester was partially prevented by axotomy or by GHBA when the reductions were calculated in percent. The findings indicate a similar mode of action of axotomy and of GHBA on the brain dopamine. (Author abstract modified)

171623 Modigh, K.; Anden, N.-E. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Effects of p-chlorophenylalanine (PCPA) and nialamide on 5-hydroxytryptamine (5-HT) in the transected spinal cord.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):28, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of p-chlorophenylalanine (PCPA) and nialamide on 5-hydroxytryptamine (5-HT) in the transected spinal cord were reported. Treatment with the monoamine oxidase inhibitor nialamide produced in the caudal part of the spinal cord an accumulation of 5-HT which was of about the same magnitude in intact and in spinalized rats. The nialamide induced increase in 5-HT was slightly but significantly smaller 2 days after transection indicating a beginning loss of synthetizing enzymes. Treatment with the tryptophan hydroxylase inhibitor PCPA caused a reduction of the 5-HT by about 70% in the cranial part of the spinal cord and in the caudal part of the intact cord but by only 30% in the caudal part of the cut spinal cord. The findings show that the nerve impulse flow is important for the PCPA induced disappearance of 5-HT but not for the nialamide induced accumulation of 5-HT. (Author abstract modified)

171624 Tissari, Anja H.; Suurhasko, Birgit V. A. Deparment of Pharmacology, University of Helsinki, 00170 Helsinki 17, Finland **Effect of imipramine on the turnover of brain 5HT in postnatal rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):29, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effect of some drugs which decrease the turnover of brain 5-hydroxytryptamine was reported. In adult rats after the administration of imipramine (IM) or chlorimipramine brain 5-hydroxyindole acetic acid (HIAA) levels were 80%, 88% and 87% of control. After similar pretreatments, increases of brain 5HIAA content following the administration of probenecid (PROB) were 56%, 56% and 72% of control. After the administration of IM to 1-day-old rats the brain 5HIAA contents were 90% and 93% of control. After the administration of N,N-dimethyltryptamine (DMT) the 5HIAA and 5HT contents of adult rat brain were 59% and 137% of control and those of 1-day-old rat brain 100% and 137%. The lack of effect of IM and DMT in 1-day-old rats suggests increase of their brain 5HT content after monoamine oxidase block and a lack

of 5HT terminals or immaturity of interneurons mediating feedback. (Author abstract modified)

171626 Sedvall, Goran; Dailey, John; Sjoquist, Birgitta. Department of Pharmacology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden **Levels of HVA in mouse brain following treatment with metabolites of chlorpromazine.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):33, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, levels of homovanillic acid (HVA) in brain of mice were reported. The effects of chlorpromazine (CPZ) and the following metabolites were studied: desmethyl-CPZ, didesmethyl-CPZ, 7-hydroxy-CPZ, CPZ-sulfoxide and CPZ-N-oxide. All the metabolites with the exception of CPZ-sulfoxide elevated markedly the level of HVA in mouse brain to about the same extent as the parent compound. All the compounds with the exception of CPZ-sulfoxide accelerated the synthesis and turnover of dopamine formed from 14C-tyrosine in mouse brain. Results demonstrate that several of the major metabolites of CPZ as all classical neuroleptics increase turnover and release of dopamine in brain. It is suggested that some CPZ metabolites have antipsychotic properties. 2 references. (Author abstract modified)

171627 Scheel-Kruger, J.; Eplov, L.; Nielsen, M. Sct. Hans Hospital, Central Laboratory, Dept. E., Roskilde, Denmark **The effect of protriptyline on the metabolism of labelled dopamine and noradrenaline in the rat brain.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):34, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effect of protriptyline on the metabolism of labelled dopamine and noradrenaline in the rat brain was reported. The biochemical analyses performed 30, 45, and 60 min after 3H-L-Dopa showed a strong decrease of labelled noradrenaline and all noradrenaline metabolites, whereas no significant effect was found on labelled dopamine or the dopamine metabolites. Specific feedback inhibition of noradrenaline biosynthesis, blockade of the uptake of 3H-L-Dopa in noradrenaline neurons or reuptake inhibition of released dopamine formed in noradrenaline neurons were discussed. (Author abstract modified)

171628 Squires, R. Research Laboratories, A/S Ferrosan, DK-2860, Soeborg, Denmark **Antagonism of p-chloroamphetamine (PCA) induced depletion of 5-HT from rat brain by some thymoleptics and other psychotropic drugs.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):35, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the 5-hydroxytryptamine (5-HT) depleting effect of d,1-p-chloroamphetamine (PCA) in rat brain antagonized by low doses of thymoleptics administered simultaneously with PCA was reported. The most potent PCA antagonists were Clorgyline and Lilly 51641 followed by chlorpheniramine and chlorimipramine, imipramine and amitriptyline and, the weakest, nortriptyline, protriptyline and desmethylimipramine. The strongest PCA antagonists gave more than 100% reversal of 5-HT depletion, while some of the weaker antagonists gave maximum reversals less than 100%. Evidence suggests that PCA, at the dose level used, is taken up into 5-HT neurones by a membrane pump which can be blocked by certain thymoleptics and chlorpheniramine. Inside the 5-HT neuron PCA both releases 5-HT and inhibits its synthesis. (Author abstract modified)

171629 Elonen, E.; Mattila, M. J. Department of Pharmacology, University of Helsinki, SF-00170, Helsinki 17, Finland **Comparison of tricyclic antidepressants as to their cardiotoxic action in conscious rabbits.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):64, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the role of noradrenaline (NA) uptake inhibition by protriptyline (PT), nortriptyline (NT), amitriptyline (AT) and doxepine (Dx) in cardiotoxicity was reported. The high efficacy of PT and NT to potentiate NA was confirmed on the rabbit's isolated right atrium. The prominent receptor blocking effect of NT, AT and Dx was confirmed on the rabbit's isolated aortic strip. Antidepressants tested immediately lowered blood pressure and increased heartrate. AT and Dx proved most potent, and they also provoked severe dysrhythmias. The results suggest that in acute experiments the cardiotoxicity of tricyclic antidepressants correlates better to their receptor blocking effect than to their effect on the NA uptake, while the latter mechanism may also be important in the long-term treatment. (Author abstract modified)

171631 von Bahr, C.; Fellenius, E.; Fried, I. Department of Pharmacology, Karolinska Institutet, S-104 01 Stockolm 60, Sweden **On the 'first-pass' effect in the liver of nortriptyline, lidocaine and propranolol.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31 (Supplement 1):92, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the first pass effect in the liver of nortriptyline (NT), lidocaine and propranolol was reported. Both lidocaine and propranolol, like NT, elicited the so called type I spectral change at much lower concentrations than most other drugs. The spectral dissociation constants indicated that all these drugs bind to P-450 with very high affinity. It is concluded that NT exhibit the FP effect in rat liver and that this might be related to a high affinity for P-450, since both NT and two other FP drugs have an unusually high affinity for this cytochrome. 1 reference. (Author abstract modified)

171632 Albanus, L.; Jonsson, M.; Norrman, S.; Osanius, B.; Sparf, B. Research Department KABI Group, Department of Pharmacology and Toxicology, S-104 25 Stockholm, Sweden **The pharmacological evaluation in laboratory animals of KABI 1702 -- a new sedative-hypnotic drug.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31 (Supplement 1):95, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, a pharmacological evaluation of KABI 1702 (gamma-Ethyl-1,2-benzisothiazoline-1,1-dioxide-3-one-2-acetamide) was reported. A decrease in motor activity in mice was found following an oral dose of about 5mg/kg and in this test KABI 1702 did not show the biphasic motor activity response which is common following barbiturate administration. Thus the sedative effect does not seem to be preceded by a phase of excitability. The effect of KABI 1702 on blood pressure and respiratory frequency is small even at hypnotic doses. The sedative effect of KABI 1702 is found following a wider dose range compared to barbiturates and a hypnotic - anesthetic stage is seen following very high doses as revealed from experiments in several species. (Author abstract modified)

171633 Kanto, J.; Pihlajamaki, K. Department of Pharmacology, University of Turku, 20520 Turku 52, Finland **Interactions of diazepam and halothane in rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):96, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the interactions of diazepam and halothane anaesthetic were reported. The plasma concentration of diazepam of the rats receiving 1.5% halothane was statistically higher at 180 minutes than in the control group. Diazepam content of liver of the rats receiving 1.5% halothane was also higher at 30 minutes and the content of liver of the rats receiving 1.5% halothane was also higher at 30 minutes and the content of N-demethyldiazepam at 60 minutes than the values of the control group. The differences in diazepam contents of blood and liver were interpreted as being due to hypotension, hypoventilation, hypoxy, and hypercapnia caused by a deep anaesthesia. It is suggested that the lipid soluble halothane might promote the flow of the lipid soluble diazepam through the blood-brain barrier. (Author abstract modified)

171634 Jonsson, J. Psychiatric Research Center, Ulleraker Hospital, S-750 17 Uppsala, Sweden **Interaction by fenfluramine with the metabolism of d-amphetamine in the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):98, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the interaction by fenfluramine with the metabolism of d-amphetamine in the rat was reported. Pretreatment with fenfluramine prolonged the excitatory behavior after d-amphetamine and increased the amphetamine levels in brain and plasma in the rat. Fenfluramine counteracted the temperature rise after d-amphetamine during the first 2 hours. Fenfluramine considerably reduced the parahydroxylation of amphetamine as indicated by a decrease of the percentage of the sum of parahydroxyamphetamine and its glucuronide and an increase of unchanged amphetamine in the urine. Norfenfluramine and N-(2-benzoyloxyethyl)-norfenfluramine (780 SE) also reduced the hydroxylated metabolites but was less active. Both fenfluramine and 780 SE accelerated the side chain metabolism of amphetamine as indicated by increased excretion of hippuric acid. Data show that norfenfluramine and its N-alkyl derivatives inhibit the aromatic hydroxylation of amphetamine. (Author abstract modified)

171785 Zigmond, R. E.; Mackay, A. V. P. MRC Neurochemical Pharmacology Unit, Dept. of Pharmacology, University of Cambridge, Medical School, Hills Road, Cambridge CB2 2QD, En-

gland **Dissociation of stimulatory and synthetic phases in the induction of tyrosine hydroxylase.** Nature (London). 247(5436):112-113, 1974.

The sequence of events that occurs between the injection of reserpine and the increase in the activity of tyrosine hydroxylase (T-OH) in the superior cervical ganglion of the rat was studied. A combination of in vivo administration of reserpine with subsequent in vitro maintenance of superior cervical ganglia was used to achieve a temporal dissociation of the transsynaptic stimulation of the ganglia from the actual increase in T-OH activity. The system was also used to assess the importance of continuing protein syntheses in the ganglion for the development of this increase in enzyme activity. It was found that any stimulation of the ganglion in the intact animal beyond that achieved within 24 hours of a single injection of reserpine is unimportant to the expression of increased T-OH activity and that the inhibition of protein synthesis in the isolated ganglion abolished the reserpine stimulated rise in T-OH activity, demonstrating that an important site of this effect of protein synthesis inhibitors is the ganglion itself. 10 references.

171904 Reinis, S. University of Waterloo, Waterloo, Ontario, Canada **Lack of effect of ribaminol, TCAP, and magnesium pemoline on recovery from neocerebellar damage.** Bulletin of the Psychonomic Society. 2(6A):385-386, 1973.

The lack of effect of ribaminol, 1,1,3-tricyano-2-amino-1-propere (TCAP), and magnesium pemoline on recovery from neocerebellar damage in mice is reported. The neocerebellar cortex lesion in newborn mice caused permanent asymmetry of the position of the hind limbs which was normalized spontaneously in about 27.8% of control animals. The administration of ribaminol, TCAP, and magnesium pemoline during the first 2 weeks of postnatal life did not improve the rate of recovery from the neocerebellar damage. 8 references. (Author abstract)

171973 Strada, S. J.; Sulser, F. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Effect of monoamine oxidase inhibitors on metabolism and in vivo release of H3-norepinephrine from the hypothalamus.** European Journal of Pharmacology (Amsterdam). 18(3):303-308, 1972.

The effect of monoamine oxidase (MAO) inhibitors on metabolism and in vivo release of H3-norepinephrine from the hypothalamus was studied in rats. Both the irreversible MAO inhibitor pargyline and the reversible inhibitor BW 63-307 (2-chloro-4-acetylamino benzonitrile) decreased radioactivity respectively while not significantly altering the release of total radioactivity into the perfusate. Thus, in animals pretreated with either pargyline or BW 63-307, practically all the radioactivity released into the perfusate consisted of norepinephrine and normetanephrine. The argument that the increased availability of norepinephrine in the perfusate could merely reflect increased sympathetic activity rather than inhibition of MAO, is weakened because BW 63-307 did not elicit gross behavioral activation or sympathetic stimulation. The results support the view that an increase in the tissue levels of endogenous or exogenous norepinephrine accompanying the inhibition of MAO results in a spillover of norepinephrine onto adrenergic receptor sites. 26 references. (Author abstract modified)

172015 Gallager, Dorothy Ann Worthington. Vanderbilt University **Serotonergic mechanisms in the central action of psychotropic drugs. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-25048 HC$10.00 MF$4.00 191 p.

A push - pull cannula was used for in vivo perfusion of a topographically localized area of the rat brain in an attempt to gather information concerning drug induced modifications of the availability of 5HT at central serotonergic effector sites. Specifically, the use of 3H-5HT in brain was evaluated and proven to be a valid marker for the endogenous amine when intraventricularly administered. Some modifications of the push - pull cannula system were then made to permit monitoring dynamic aspects of the serotonergic system in the unanesthetized rat, with the dorsal hippocampus as the site of perfusion. Support was obtained for the hypothesis that the availability of 5HT at receptor sites is increased by reserpine like drugs, at least during the phase of the rapidly declining stores. Direct evidence that inhibition of monoamine oxidase (MAO) increases the amount of 5HT in the perfusate, while reducing 5HIAA (the metabolite of 3H-5HT) to negligible amounts. The slower rate of decline of radioactivity in the hippocampus perfusate following administration of chlorimipramine suggested an increased availability of 5HT at serotonergic receptor sites and is consistent with the hypothesis that the drug blocks the reuptake of 5HT at the neuronal mem-

brane. Finally, results provided the first direct demonstration that p-chloroamphetamine release 5HT in brain at early time periods after drug administration. (Journal abstract modified)

172017 McKernan, John Barry. University of Alabama in Birmingham Medical Center **Influence of phenobarbital and sex hormones on enzymes in ascorbic acid biosynthesis in male and female rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27272 HC$10.00 MF$4.00 65 p.

Further investigation was made of research findings of increased ascorbic acid excretion in male rats following phenobarbital administration, an effect attributed to increase in UDP-glucose dehydrogenase activity despite decreased activities of gulonate-NADP-oxidoreductase and gulonolactone-02-oxidoreductase, two of the four enzymes in the ascorbate biosynthetic pathway. Specifically, apparent sexual differences of the four ascorbate biosynthetic enzymes were investigated in male and female Sprague-Dawley rats. In males, gulonolactone hydrolase and gulonolactone-02-oxidoreductase had decreased enzyme activity, while glucuronolactone hydrolase and gulonate-NADP-oxidoreductase activity was unchanged. In females, gulonolactone-02-oxidoreductase had decreased enzyme activity; gulonate-NADP-oxidoreductase and gulonolactone hydrolase remained unchanged, while glucuronolactone hydrolase increased two fold in activity. Since an endocrine basis for the sexual difference following phenobarbital treatment seemed likely, the activities of the four ascorbate enzymes were analyzed in castrate male and female rats. Some differences were noted as a result of estrogen phenobarbital administration to ovariectomized females and testosterone phenobarbital administration to castrate males, as compared to normals, while other enzyme activities remained unchanged. (Journal abstract modified)

172018 Oh, Young-Ja Park. University of Minnesota **Determination of drug transfer across biological membranes: comparative study on the passage of drugs into the central nervous system and their placental transfer and fetal localization in the pregnant rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-25697 HC$10.00 MF$4.00 155 p.

The relationship between drug transfer rates across the placenta and their physicochemical characteristics were investigated in pregnant rats after single I.V. injection and steady state infusion of drugs. Chemically dissimilar (group one) and similar (group two) drugs were studied in vivo to determine whether any pharmacokinetic differences in drug transport exist across the blood-brain barrier and placental membrane. In single pulse injection studies, brain tissues were generally less permeable to drugs than other tissues. The time - concentration curve developed by the placenta had a unique pattern in that the early passage of nearly every drug was retarded. In both single and steady state infusion studies, the general drug dispostion patterns identified for structurally dissimilar compounds did not reliably predict their pharmacokinetic behavior, while the patterns were very reliable predictors for structurally similar compounds. The intercept of the linear regression equations reflected the degree of accessibility and/or affinity of a given tissue to drugs. Most drugs were poorly distributed to the fetal brain and liver and the maternal brain as compared to maternal liver and placenta. These low concentrations are due to differences in the anatomic relationships and biochemical constituents of these tissues. (Journal abstract modified)

172019 Patrick, Graham Abner. University of North Carolina at Chapel Hill **Effects of centrally acting drugs on adenyl cyclase activity and cyclic AMP levels of mouse brain. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-26223 HC$10.00 MF$4.00 109 p.

The effects of centrally acting drugs on brain adenyl cyclase activity and adenosine 3',5'-cyclic monophosphate (cyclic AMP) were investigated to determine whether these drugs might exert their pharmacologic actions through effects on the brain cyclic AMP system. The narcotic analgesic, morphine, and the narcotic antagonist, maxolone, produced little or no evidence of any effect on brain cyclic AMP. The phenothiazine major tranquilizers and the tricyclic antidepressants generally produced a biphasic effect of adenyl cyclase activity in vitro, causing stimulation at lower concentrations and inhibition at higher concentrations. In vivo, tricyclic drugs decreased brain cyclic AMP levels following decapitation. Major tranquilizers of the tetrabenazine type produced inhibitory actions similar to those of the phenothiazines on adenyl cyclase and cyclic AMP, but were considerably less potent. The

natural cannabinoids produced no significant effects, but two synthetic cannabinol analogues produced significant effects on adenyl cyclase activity in vitro. Results point to possible involvement of the brain cyclic AMP system in the central actions of the phenothiazine tranquilizers, tricyclic depressants, and certain cannabinol analogues. (Journal abstract modified)

172020 Winston, Reed Alan. University of Rochester **Cortical synaptosomal uptake and subsynaptosomal distribution of 3H-norepinephrine and 3H-amphetamine: modification by tricyclic and psychoactive agents in vitro. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-26561 HC$10.00 MF$4.00 128 p.

The uptake and subsynaptosomal distribution of 3H-amphetamine and 3H-norepinephrine distribution in the rat cerebral cortex were studied, along with the effects of tricyclic and psychoactive agents in vitro, in an attempt to isolate a binding substance for norepinephrine. Specific experiments were conducted using amitriptyline, chlorpromazine, desipramine, imipramine, lithium carbonate and protriptyline. The effects of these compounds on uptake and subsynaptosomal distribution of 3H-amphetamine and 3H-norepinephrine, as well as the effects of the agents on the subsynaptosomal metabolism of 3H-norepinephrine, are reported. (Journal abstract modified)

172021 Jackson, Fabian Broadway. Wake Forest University, The Bowman Gray School of Medicine **The role of the septal area of the brain in the inhibitory modulation of behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-25419 HC$10.00 MF$4.00 160 p.

The hypothesis that the modulating role of a forebrain, particularly the septum, is correlated with its level of integrative capability was investigated in male Sprague-Dawley rats. Ss were initially trained on an operant schedule for 30 sessions, and then given septal lesions, sham operations or were left unchanged. The effects of chlorpromazine, a central catecholamine blocker, and amphetamine, which apparently increases arousal levels by acting on the midbrain reticular system, on the three groups of Ss were also investigated. Subsequent to DRL training, groups were compared on two tests of simple locomotor activity. Overall results indicate that the septal area encompasses two separate inhibitory systems which regulate operant responding. One functions at moderate arousal levels and is related to the medial septal - hippocampal cholinergic pathway. The second functions at high arousal levels and is not related to the medial - hippocampal system. No modulatory systems regulating simple locomotor activity could be demonstrated in the septum. Rather, controls for this behavior appeared to run in lower diencephalic areas. (Journal abstract modified)

172596 Gill, E. W.; Lawrence, D. K. University Dept. of Pharmacology, South Parks Road, Oxford, UK **The distribution of delta1-tetrahydrocannabinol and 7-hydroxy-delta1-tetrahydrocannabinol in the mouse brain after intraventricular injection.** Journal of Pharmacy and Pharmacology. 25(12):948-952, 1973.

Delta1-tetrahydrocannabinol (delta1-THC) and 7-hydroxy-delta1-THC were injected into the cerebral ventricles of mice by an improved technique, and the potencies of the drugs were measured by the mouse catalepsy test. Both drugs were found to have the same activity when administered by this route as after intravenous injection. Autoradiographic experiments with tritium labelled compounds showed that at the time of the peak behavioral effect almost all the injected dose remained in the intraventricular space, and had not penetrated the brain. Delta1-THC was found to remain in the ventricles after the behavioral effect had disappeared. 20 references. (Author abstract modified)

172599 Haavik, Coryce O.; Hardman, Harold F. Dept. of Pharmacology, Medical College of Wisconsin, Milwaukee, WI 53233 **Hypothermic action of delta9-tetrahydrocannabinol, 11-hydroxy-delta9-tetrahydrocannabinol and 11-hydroxy-delta8-tetrahydrocannabinol in mice.** Life Sciences (Oxford). 13(12):1771-1778, 1973.

The hypothermic activity of delta9-tetrahydrocannabinol (delta9-THC), a metabolite, 11-hydroxy-delta9-THC (11-OH-delta9-THC) and 11-OH-delta8-THC has been determined in male mice maintained at an ambient temperature of 200 1 degree C. The mean body temperature of mice that received 2, 4, 16, or 32 mg/kg, i.v.,of a THC was significantly lower than that of vehicle treated mice within 2 minutes after drug administration. Dose - response relationships show the intrinsic activity of delta9-THC to be significantly greater than that of 11-OH-delta9-THC or 11-OH-

delta8-THC in this system. 10 references. (Author abstract)

172749 Guerrero-Figueroa, R.; Guerrero-Figueroa, E.; Sneed, Gary A.; Gallant, D. M. Dept. of Psychiatry and Neurology, Tulane Univ. School of Medicine, New Orleans, LA **Effects of molindone on CNS structures: neurophysiological and behavioral correlations.** Current Therapeutic Research. 15(7):508-519, 1973.

The effects of molindone (M), a dihydroinolone derivative, on electroencephalogram and multiunit spontaneous activity and on local evoked potentials (LEP) recorded from subcortical and cortical structures of normal and epileptic cats and monkeys are reported. Molindone produced in limbic system structures the following electrographic changes: augmentation in the amplitude of the postsynaptic components of the LEP; an increase in the firing rate of extracellular unit activity, and an increase in the amplitude of voltage. Response differences to lowest and highest dose levels are noted. In animals with subcortical and/or cortical epileptogenic tissues, Molindone produced activation of primary and secondary epileptiform discharges. Behavioral changes were characterized by an initial state of excitation followed by a state of depression. 18 references. (Journal abstract modified)

172780 Croucher, T.; Hindmarch, I. Dept. of Psychology, Univ. of Leeds, Leeds, England **The spiral after effect (SAE) as a measure of motion sickness susceptibility and the effect on the SAE of an antimotion sickness drug and a central nervous system depressant.** Psychopharmacologia (Berlin). 32(3):215-222, 1973.

Whether the spiral after effect (SAE) could be considered a reliable measure of motion sickness susceptibility as measure by Reason's motion sickness questionnaire (MSQ) was studied. In an initial correlation study it was found that MSQ scores were correlated with neuroticism scores on the Eysenck Personality Inventory. The correlation between MSQ and a measure of the SAE duration was not significant. In the subsequent controlled drug study it was shown that both dimenhydrinate-an antinauseant, and temazepam-a minor tranquillizer decreased the duration of SAE, although significance was only obtained with the latter drug. Results are fully discussed and it is suggested that SAE has both a cortical and vestibular component in its mechanism of action. 18 references. (Author abstract modified)

172835 Herbaczynska-Cedro, Krystyna. Experimental and Clinical Medical Research Center, Polish Academy of Sciences, Dworkowa Str. No. 3, Warswa, Poland **Some aspects of respiratory control in neuroleptoanalgesia.** Acta Physiologica Polonica (Warszawa). 23(3):333-345, 1972.

The evaluation of the activity of respiratory centers in the state of neuroleptoanalgesia (NLA) was related to central and peripheral regulation of breathing. Experiments were performed on 40 rabbits. The pattern of bioelectric activity of phrenic nerves was recorded. The evolution of basic responses of the respiratory system in NLA type-II was studied. The effect of preparations composing the mixture NLA-II (Fantanyl and Dehydrobenzperidol) on the respiratory rhythm and on the effect of hyperventilation was evaluated. Preliminary investigations were carried out on the respiratory system response to carbon dioxide in NLA. The results confirm the existence of different responses of the respiratory control system, related to the depth of general anesthesia and the kind of anesthetic applied. It was concluded that the NLA maintained the functional state of respiratory neurones at a level similar to that observed in other types of superficial anesthesia. 27 references. (Journal abstract modified)

172915 Dyer, Donald C.; Nichols, David E.; Rusterholz, David B.; Barfknecht, Charles F. Anesthesia Research Center, School of Medicine, University of Washington, Seattle, WA 98195 **Comparative effects of stereoisomers of psychotomimetic phenylisopropylamines.** Life Sciences (Oxford). 13(7):885-896, 1973.

Stereoisomers, R(-) and S(+) of five psychotomimetic phenylisopropylamines contracted isolated strips of sheep unbilical arteries. The compounds exhibited the following order of potency: 2,5-dimethoxy-4-bromo-amphetamine (DOB) greater than 2,5-dimethoxy-4-ethyl-amphetamine (DOET) greater than 2,5-dimethoxy-4-methylamphetamine (DOM) greater than 2,5-dimethoxy-amphetamine (2,5-DMA) greater than 4-methoxy-amphetamine (PMA). Stereoselectivity was observed in that the R(-) isomers were more active than the S(+) isomers except for PMA. Evidence was obtained for the action of these hallucinogens on 5-hydroxytryptamine receptors. There was a general correlation of smooth muscle stimulating activity with known hallucinogenic activity. 12 references. (Author abstract)

172916 Gutierroz C., Orlando; Spiguel, Rodolfo D. Departamento de Psiquiatria, y Salud Mental, Escuela de Medicina, Universidad de Chile, Casilla 6589, Santiago, Chile **Oscillatory potentials of the cat retina: effects of adrenergic drugs.** Life Sciences (Oxford). 13(7):991-999, 1973.

The effects of L-DOPA on the electroretinogram (ERG) of a previously reserpinized cat are reported. When reserpine was used as a monoaminergic depletion agent, a diminution or suppression of certain components of the oscillatory potentials of the ERG were observed. L-DOPA administration to reserpinized cats restored the altered oscillatory potentials (OP) components. The possible interference of systemic disturbances provoked by the drugs was studied via artificial variations of blood pressures. Results suggest that reserpine and L-DOPA are acting on catecholamine dependent retinal structures, probably the dopamine containing population of amacrine cells. An hypothesis is advanced concerning the possible role of tangential structures in the generation of the oscillatory potentials of the retina. 24 references. (Author abstract)

172917 Maitre, L.; Waldmeier, P. C.; Baumann, P. A. CIBA-GEIGY Ltd., Basel, Switzerland **Effects of some tetrahydrocannabinols on the biosynthesis and utilization of catecholamines in the rat brain.** Life Sciences (Oxford). 13(7):cxii-cxv, 1973.

On the assumption that catecholamines may be involved in the central effects of the tetrahydrocannabinols (THCs), the effects of these compounds on the biosynthesis and use of catecholamines in the rat brain were studied in four experiments. These were studies of: 1) accumulation of 3H-catecholamines in the whole brain following administration of delta9-THC, delta8-THC, or dimethylheptyltetrahydrocannabinol (DMHP); 2) accumulation of 3H-catecholamines in different brain regions following administration of these compounds; 3) the disappearance of newly synthesized 3H-catecholamines from the whole brain following THC administration; and 4) disappearance of newly synthesized 3H-catecholamines from different brain regions following THC administration.

172923 Meyer, H.; Frey, H. -H. Department of Pharmacology and Toxicology, School of Veterinary Medicine, Free University, Berlin, Germany **Dependence of anticonvulsant drug action on central monoamines.** Neuropharmacology (Oxford). 12(10):939-947, 1973.

The influence of receptor blocking drugs and variations in the central levels and metabolism of noradrenaline, dopamine, and 5-hydroxytryptamine (5-HT) on the effect of anticonvulsant drugs in mice was studied. The effect of phenobarbital against electroconvulsions was antagonized by treatments lowering central 5-HT or noradrenaline, as well as by cyproheptadine and phentolamine. A synergistic effect occurred from 5-hydroxytryptophan (5-HTP) and L-DOPA. The anticonvulsant activity of diphenylhydantoin in the maximal electroshock seizure test decreased after treatment with alpha-methyl-tyrosine and disulfiram; noradenaline thus plays a role in the drug's effect, while participation of 5-HT remains doubtful. In the pentetrazole seizure threshold test, phenobarbital was antagonized by p-chlorophenylalanine and cyproheptadine, whereas 5-HTP had a synergistic effect, thereby proving participation of 5-HT in mediation of the anticonvulsant action of the drug while participation of noradrenaline is unlikely. Results with ethosuximide were similar regarding the role of 5-HT, but experiments on the role of catecholamines gave conflicting results. It appears that changes in anticonvulsant ED50 values induced by interferences with the central monoamines do not merely follow the simultaneous changes in convulsive threshold. 27 references. (Author abstract modified)

172924 Dowson, J. H. Dept. of Psychiatry, Royal Edinburgh Hospital, Edinburgh 10, Scotland **Quantitative histochemical studies of striatal dopamine depletion following DL-alpha-methyl-p-tyrosine administration.** Neuropharmacology (Oxford). 12(10):949-953, 1973.

The use of a microfluorimetric histochemical method for measuring depletion of dopamine in the rat caudate nucleus, following alpha-methyl-p-tyrosine (alpha-MT) administration, was investigated. The depletion in three behavioral situations was compared with that of a control group which remained in a cage. Results for controls indicate a reduction of approximately 50% in intensity of formaldehyde induced fluorescence derived from dopamine in a region of the neuropil of the caudate nucleus, during the interval between alpha-MT, 300mg/kg i.p.,and killing. Disruption of conditioned avoidance response (CAR) performance after alpha-MT administration was confirmed, but CAR performance in previously trained rats had no significant effect on depletion of formaldehyde induced fluorescence

of the striatal neuropil after alpha-MT administration. Levels of alpha-MT induced depletion of formaldehyde induced fluorescence in the striatal neuropil following a period of muscular coordination/activity and following a period of CAR training were also not significantly different from those shown by a control group. 12 references. (Author abstract)

172925 Goodman, F. R.; Weiss, G. B. Department of Pharmacology, University of Texas Southwestern Medical School, Dallas, TX 75235 **Alteration of 5-hydroxytryptamine-14C efflux by nicotine in rat brain area slices.** Neuropharmacology (Oxford). 12(10):955-965, 1973.

The manner in which nicotine affects the distribution and metabolism of 14C labelled serotonin (5-HT-14C) in rat brain slices prepared from cerebellum, cortex, striatum, and hypothalamus was investigated. Tissue spaces occupied by 5-HT-14C were measured for differing incubation intervals and temperatures. In all preparations, the total 14C space values at 37 deg C were higher than at 23 deg or 0 deg C. Pheniprazine and procaine (but not nicotine) at 37 deg C markedly increased the concentration of 5-HT-14C and decreased that of 14C-labelled metabolities (principally 5-HIAA-14C). Addition of procaine, high potassium ion or nicotine increased 5-HT-14C efflux in striatum and hypothalamus slices, but only the effect of potassium was transient. Omission of Ca2+ from the bathing solution inhibited the increase in 5-HT-14C efflux obtained with potassium, but not that with nicotine. Addition of nicotine also decreased 22Na efflux. Removal of sodium ion prevented the nicotine induced increase (but not the K+ induced increase) in 5-HT-14C efflux. Thus, nicotine may indirectly alter 5-HT-14C movements by affecting one or more Na+ dependent reactions important for 5-HT transport. 31 references. (Author abstract)

172926 Jurna, I.; Grossmann, W.; Theres, C. Institut fur Pharmakologie and Toxikologie der Universitat des Saarlandes, Abteilung fur Neuropharmakologie, D-665 Homburg/Saar, Germany **Inhibition by morphine of repetitive activation of cat spinal motoneurones.** Neuropharmacology (Oxford). 12(10):983-993, 1973.

Spinal motoneurones and interneurones were investigated by intracellular and extracellular microelectrode recording in spinal cats. Morphine (2mg/kg) and the morphine antagonist levallorphan (0.2mg/kg) were injected intravenously. Results are: 1) the action potentials evoked in motoneurones by ventral root stimulation were not changed in amplitude, duration and rates of rise and fall; 2) polysynaptic excitatory postsynaptic potentials (EPSPs) elicited by stimulating dorsal roots with single pulses were depressed, whereas monosynaptic EPSOs were generally unchanged; 3) the inhibitory postsynaptic potentials (IPSPs) evoked in gastrocnemius-soleus motoneurones by sural nerve stimulation were scarcely affected; 4) the repetitive discharge from interneurones located near motoneurones was reduced; 5) temporal facilitation of EPSPs produced in motoneurones by repetitive stimulation of Ia afferents from the gastrocnemius-soleus muscles was depressed by morphine and antagonized by levallorphan; and 6) the increase in excitability of terminals of Ia afferents from the gastrocnemius-soleus muscles was depressed by morphine. Results are discussed with respect to inhibition of polysynaptic mass reflexes in spinalized animals; morphine may influence processes which are generated by repetitive activation. 21 references. (Author abstract)

173029 Ritter, Sue; Stein, Larry. Department of Research and Development, Wyeth Laboratories, P.O. Box 8299, Philadelphia, PA 19101 **Self-stimulation of noradrenergic cell group (A6) in locus coeruleus of rats.** Journal of Comparative & Physiological Psychology. 85(3):443-452, 1973.

Self-stimulation of noradrenergic cell group (A6) in locus coeruleus of rats was explored. Twenty out of 21 electrodes in the almost exclusively noradrenergic cell concentrations of the locus coeruleus supported high and stable rates of self-stimulation. Locus coeruleus self-stimulation was facilitated by amphetamine and suppressed by chlorpromazine and alpha-methyl-p-tyrosine, but pimozide at relatively high doses had almost no effect. The results demonstrate that self-stimulation can be localized in a relatively homogeneous noradrenergic site and thus provide presumptive evidence that at least some noradrenergic neurons specifically mediate rewarding effects. 54 references. (Author abstract)

173133 Eissenberg, Ethel M. University of Tennessee **The curarized rat and heart rate conditioning: a consideration of respiration parameters and neuromuscular blocking agents in a classical conditioning paradigm. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27723 HC$10.00 MF$4.00 185 p.

An attempt was made to overcome difficulties in replicating instrumental cardiovascular phenomena in curarized rats due to the instability of the curarized preparation by considering respiration parameters and neuromuscular blocking agents in a classical conditioning paradigm. Chest movements were maintained at a constant amplitude by adjusting peak inspiration pressure (PIP) values and four different I:E ratios were investigated. The consistency and magnitude of heartrate responses to tone and shock stimulation under these conditions support use of these respiration procedures in preference to the traditional ones of constant pressure respiration with a 1:1 I:E ratio. Given a stable preparation, it was considered imperative to demonstrate classical conditioning in the curarized preparation prior to further attempts to operantly condition cardiovascular responses. To this end, optimal respiration parameters were used with three experimental groups in a classical conditioning paradigm preceded by 10 presentations of conditioned stimulus (CS) alone to permit habituation of the heartrate response to tone. One group was given an initial light dose of curare, one injected with a large dose of curare, and a third was immobilized with an alternate neuromuscular blocking agent, succinylcholine chloride (Anectine). Results are reported in detail, concluding that Anectine is a feasible, if not preferable neuromuscular blocking agent for cardiovascular research with the immobilized rat. (Journal abstract modified)

173257 Wedig, John H.; Gay, Vernon L.; Midgley, A. R., Jr. Olin Research Center, 275 Winchester Ave., New Haven, CT 06504 **CNS depression in the absence of prolactin release following intraarterial injections of sodium pentothal in the proestrous rat.** Experimental Biology and Medicine. 144(3):989-992, 1973.

Central nervous system (CNS) depression in the absence of prolactin release following intraarterial injections of sodium pentothal was studied in proestrous Holtzman rats. Either pentobarbital or pentothal anesthesia maintained during the critical period in proestrus rats blocked the preovulatory increase in serum luteinizing hormone and prevented subsequent ovulation. Pentobarbital anesthesia induces a rapid increase in serum prolactin concentrations whereas pentothal does not. The mechanisms of prolactin release are not clarified but the two previously correlated sequelae of anesthesia are separated. 19 references. (Author abstract modified)

173380 Holz, R. W.; Coyle, J. T. Depts. of Pharmacology and Psychiatry, Johns Hopkins Medical School, Baltimore, MD 21205 **The inhibition of 03H0dopamine uptake into rat striatal by veratridine and batrachotoxin. (Unpublished paper).** Bethesda, MD, NIMH, 1974, 19 p.

Veratridine and batrachotoxin increase the Na+ permeability of excitable membranes and inhibit 03H0-dopamine uptake into synaptosomes prepared from rat striatum; these effects can be prevented by tetrodotoxin, a special blocker of Na+ channels. Results suggest that the inhibition of uptake by veratridine and batrachotoxin is caused by an increased Na+ permeability of the synaptosomal membrane. Further evidence suggests that the inhibition of influx of dopamine by veratridine and batrachotoxin is primarily a result of an increased Na+ or a decreased K+ concentration within the synaptosome. These results are consistent with the hypothesis that ions are cotransported with dopamine across the synaptosomal membrane. 18 references. (Author abstract modified)

173381 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Drug induced activation of striatal tyrosine hydroxylase: changes in the affinity for pteridine cofactors. (Unpublished paper).** Washington, DC, NIMH, 1974, 13 p.

Drug induced activation of striatal tyrosone hydroxylase (TH) was studied in rats to determine changes in the affinity for pteridine cofactors. A single intraperitoneal injection of haloperidol, methiothepin, pimozide, and reserpine promptly increases TH activity of striatal homogenate, but not that of hypothalamus, brain stem and adrenal gland. Pretreatment of rats with cycloheximide fails to change the increase of TH elicited by methiothepin or reserpine. Apomorphine and trivastal fail to change striatal TH but abolish the increase elicited by methiothepin. These drugs also significantly reduce the increase of TH caused by reserpine. Haloperidol, methiothepin and pimozide increase only TH associated with supernatant, but the particle bound TH remains unchanged. Results suggest that striatal TH can be regulated in vivo by a change of the Km for the pteridin cofactor. 36 references. (Author abstract modified)

173382 Saavedra, J. M. National Institutes of Health, Bethesda, MD 20014 **Measurement of**

biogenic amines at the picogram level. (Unpublished level). Bethesda, MD, NIMH, 1974, 12 p.

A number of enzymatic - isotopic methods for the assay of biogenic amines at the picogram level are described. These assays allow the measurement of dopamine, norepinephrine, histamine, beta-phenylethylamine, octopamine, phenylethanolamine, serotonin, N-acetylserotonin, and tryptamine in small areas of the brain and in body fluids. They are useful to determine the concentrations of putative neurotransmitters in individual brain nuclei of the rat brain, in isolated neurons from molluscs, and to study low levels of biogenic amines in human plasma under different physiological and pathological conditions. 18 references. (Author abstract modified)

173387 Murphy, Dennis L. Laboratory of Clincal Science, NIMH, Bethesda, MD 20014 **Technical strategies for the study of catecholamines in man. (Unpublished paper).** Bethesda, MD, NIMH, 1974, 12 p.

Attempts to study catecholamines, catecholamine related enzymes and catecholamine transport, storage and release mechanisms at the cellular level in man are discussed. Examples from current studies at NIMH are used for illustration. Investigations of biogenic amine enzymes, transport and metabolic functions, and receptor effects of amines in human cells suggest a potential for the use of such approaches in confirming amine metabolic changes studied by other techniques, and in determining individual differences in response to amine affecting drugs. 47 references.

173398 Gillin, J. Christian; Cannon, Eleanor; Magyar, Regis; Schwartz, Michael; Wyatt, Richard J. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeth's Hospital, Washington, DC **Failure of N,N-dimethyltryptamine to evoke tolerance in cats.** Biological Psychiatry. 7(3):213-220, 1973.

N,N-dimethyltryptamine (DMT) was administered to five male cats twice daily for 7 to 15 days and to four cats every 2 hours for 24 hours to determine whether tolerance to DMT would develop. Results indicate that tolerance did not develop to DMT when given either twice daily for 7 to 15 days or every 2 hours for 24 hours. Repeated administration of DMT produced consistent changes in coordination, posture, pupil dilatation, propensity for vomiting, staring, apparent hallucinations, and electroencephalogram (EEG). No long lasting effects were noted when DMT administration was discontinued. In contrast, tolerance to lysergic acid diethylamine (LSD) developed quickly as measured by changes in EEG, pupil dilatation, staring, and apparent hallucinatory behavior. Results indicate that LSD and DMT may act by different mechanisms. Present results are consistent with a model of schizophrenia which hypothesizes that DMT is a continuously synthesized endogenous psychotogen to which tolerance does not develop. 21 references.

173588 Nichols, David Earl. University of Iowa **Potential psychotomimetics: bromomethoxyamphetamines and structural congeners of lysergic acid. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-30961 HC$10.00 MF$4.00 191 p.

Consideration of various structural elements in LSD led to the proposal that a phenethylamine moeity may be the active pharmacophore, and the hypothesis that LSD may act at two separate receptors in the brain was developed and tested. The LSD D-ring was considered as the other potentially active portion of the molecule. Dopaminergic receptors were proposed as one possible site of action; 5-HT or adrenergic sites as the others. Six bromomethoxyamphetamines were synthesized and tested in rats for an effect on the conditioned avoidance response. Results showed that psychotomimetic activity resided only in compounds with a para bromine. Comparison of activity data with values for fluorescence intensity and with HOMO values for the corresponding chloromethoxyamphetamines indicated that no correlations exist, and it is concluded that the para substituent has most importance in conferring metabolic stability on the molecule. The importance of stereochemistry of the methoxylated amphetamines is also stressed, and a rigid analog of DOM (STP) was prepared as an LSD AC-ring congener. Finally, attempts were made to prepare N-methyl-5-carbethoxy-3-piperidone as an intermediate for synthesis of substituted 3-phenyl-1,2,5,6-tetrahydropyridine-5-carboxylic acid derivatives as LSD AD-ring congeners. (Journal abstract modified)

173601 Moldowan, Mervin John. University of British Columbia, Canada **Kinetics and cellular control mechanisms for imipramine metabolism in**

the isolated perfused rat liver. (Ph.D. dissertation). Dissertation Abstracts International. Ottawa, Canada, National Library of Canada at Ottawa, 1973.

The kinetics and possible cellular control mechanisms for imipramine HC1 metabolism in the isolated perfused rat liver were investigated. The isotope 14C-imipramine was used and quantification was done by liquid scintillation counting. Analysis for imipramine (IMI), desmethylimipramine (DMI), free hydroxy (OH), glucuronide (G), and N-oxide (N-O) metabolites was done on the perfusate, bile and liver. Overall findings suggest that optimal conditions were established to study possible cellular control mechanisms for IMI metabolism in the isolated perfused rat liver. Dibutyryl cyclic AMP caused inhibition of IMI metabolism. DMI formation was inhibited 28% while GOH formation was inhibited 29%. NADPH or NADH inhibited imipramine metabolism GOH and DMI were both inhibited. Succinic acid inhibited DMI formation, but not GOH. (Journal abstract modified)

173775 Wolgin, David L. Rutgers University -- The State University of New Jersey **An analysis of tolerance to the anorexigenic effects of amphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27996 HC$10.00 MF$4.00 90 p.

The role of anorexigenic effects of amphetamine in development of tolerance was investigated in rats, defining tolerance as the attenuation of the initial anorexigenic effects as a function of the drug's chronic administration. In one experiment, Ss made tolerant to a 3.0mg/kg dose did not display a concomitant decrease in responsivity to a 1.5mg/kg dose, and many Ss actually displayed a lower intake following the lower dose, while Ss made tolerant to the lower dose did not display a decreased responsivity to a 0.75mg/kg dose. This pattern of results may be related to the initial differences in responsivity to each pair of doses before the development of tolerance. In experiment two, Ss made tolerant to the suppressant effect of amphetamine on milk intake were offered various other substances following either amphetamine or saline. Results suggest that tolerance is not simply due to adaptation to drug induced stimuli, but many may involve instead adaptation to both drug induced and food related cues. Taken together, findings indicate that palatability of the food given under the drug and adaptation to both drug induced and food related stimuli are important in development of tolerance to the anorexigenic effects of amphetamine. (Journal abstract modified)

173872 Wei, Eddie; Loh, Horace. School of Public Health, University of California, Berkeley, CA **Morphine physical dependence unaltered by previous dependence on morphine.** Nature (London). 238(5364):396-397, 1972.

Morphine dependence in the rat was studied to determine if previous exposure to morphine permanently alters the neural substrates for producing physical dependence on morphine. Early dependence on morphine was not found to intensify the dependence produced by subsequent exposure to morphine as measured by behavioral parameters and body weight loss during naloxone precipitated withdrawal. 14 references.

173875 Melikian, A. P.; Forrest, I. S. Department of Psychiatry, Stanford University School of Medicine, Stanford, CA **In vivo 3H-prochlorperazine metabolism in the guinea pig and rabbit.** Proceedings of the Western Pharmacological Society. 15(78):15:78-82, 1972.

In vivo 3H-prochlorperazine metabolism was examined in the guinea pig and the rabbit. Both rats and guinea pigs required the same period of time for total urinary and fecal excretion of chlorpromazine and prochlorperazine but the dominant routes of excretion of the two drugs were found to differ. Both species excreted chlorpromazine primarily via the urine, but eliminated prochlorperazine predominantly via the feces; this difference appeared to be due exclusively to the side-chain. A lack of absorption of the piperazine linked drug did not appear to account for the difference in elimination since both species showed a wide range of fecal drug metabolites. 12 references.

174036 Bennett, Edward L.; Rosenzweig, Mark R.; Wu, Su-Yu Chang. Lawrence Berkeley Laboratory, University of California, Berkeley, CA 94720 **Excitant and depressant drugs modulate effects of environment on brain weight and cholinesterases.** Psychopharmacologia (Berlin). 33(4):309-328, 1973.

The hypothesis that certain excitant drugs can enhance the effects of enriched experience on brain measures was tested. Most experiments were performed with prepubertal male rats. Some rats were exposed in groups of 12 to an enriched

environmental condition (EC). Others remained in their individual home cages (HC) throughout. Methamphetamine and d-amphetamine enhanced the EC effects; metrazol had small positive effects, and strychnine was without effect. Phenobarbital depressed the brain weight effects but increased the enzymatic effects. Use of methamphetamine made it possible to find EC effects with short daily periods or with a shortened experimental duration. In experiments with adult rats, methamphetamine did not modulate the brain weight effects. The results may bear on the use of stimulants to promote recovery from brain damage. 24 references. (Author abstract modified)

174257 Bandman, A. L.; Smirnova, L. V.; Sofronov, G. A. S. M. Kirov Military Medical Academy, Leningrad, USSR **/The effect of psychotropic agents on some aspects of acetylcholine metabolism in cat brains./** Vliyaniye psikhotropnykh sredstv na nekotoryye storony obmena atsetilkholina v golovnom mozge koshek. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(7):56-58, 1973.

Results of experiments performed on cats to study the synthesis, release, and level of acetylcholine in the large hemisphere cortex of cats are tabulated. The procedure is described in detail. Amizyl was found to increase the release of acetylcholine by the brain cortex and to diminish the content of bound mediator fraction in the cortex of large hemispheres and the midbrain. Chlorpromazine increased the release and elevated the content of free acetylcholine in the tissues of the cortex and the midbrain. The intensity of release of the mediator decreased under the effect of tryphthazine, and the free fraction in the cortex increased. 11 references.

174318 Gabay, Sabit. Biochemical Research Laboratory, Veterans Administration Hospital, Brockton, MA 02401 **An enzyme approach in appraising the mode of some tranquilizers and antidepressants.** Texas Reports on Biology and Medicine. 31(3):295-310, 1973.

The interaction of certain tranquilizers and antidepressants were investigated in isolated systems using an enzyme approach. Specifically, the interactions of the following neuropsychiatric agents were examined: (1) flavin dependent enzymes and phenothiazines, such as D-amino acid oxidase (D-AAO), and (2) purified monoamine oxidase (MAO) and some antidepressants (MAO inhibitors). In testing the mode of action of the phenothiazines, the drugs were divided into three groups depending on the nature of their side chain: aliphatic, piperidine, or piperazine. The compounds were tested and listed in order of their decreasing inhibitory power over D-AAO. Inhibition was dependent on the protein concentration, and albumin also protected D-AAO from the inhibitory action of the drugs. The slight structural differences between the various phenothiazines have altered their capacity for binding to the enzyme. Speculation regarding the stereochemistry of the interaction of the chelating agents, tranylcypromine and thyroxine is also offered. In this case, it appears that MAO inhibition is due not so much to inactivation, but to functional transformation. Due to possible general occurrences of such a mechanism in antidepressive agents, other parameters should be investigated based on this concept. 28 references. (Author abstract modified)

174319 Willis, William D., Jr.; Ashkenazi, Ruth; Willis, Jean C.; Haber, B. Division of Comparative Marine Neurobiology, Marine Biomedical Institute, University of Texas Medical Branch, Galveston, TX 77550 **The role of monoamine oxidase in terminating the reflex effects of para-methoxyphenylethylamine (PMPEA).** Texas Reports on Biology and Medicine. 31(3):423-429, 1973.

Further evidence is provided that the drug, para-methoxyphenylethylamine (PMPEA), acts at monoaminergic synapses by demonstrating that nialamide, an inhibitor of the enzyme monoamine oxidase (MAO), causes an enhancement and prolongation of the effect of PMPEA on the monosynaptic reflex of the cat spinal cord. PMPEA was shown to compete for active sites on MAO, using 5-hydroxytryptamine or tyramine as substrates. It is suggested that the action of PMPEA is terminated by MAO, thus accounting for the relatively brief action of PMPEA on reflexes. 8 references. (Author abstract)

174603 Mori, Masahiro; Nishijima, Yoshiaki; Iwata, Noriyoshi. no address **Effect of a new psychotropic drug, CS-370 (10-Chloro-11b-(2-chlorophenyl)-2,3,5,6,7, 11b-hexahydrobenzo(6,7)-1,4-diazepino(5,4-b)oxazol-6-one) upon the central nervous system.** Annual Report of Sankyo Research Laboratories (Tokyo). 24:216-217, 1972.

The effects of the psychotropic drug, CS-370, on the central nervous system are discussed. CS-370 has the same potency as diazepam against convulsion induced by bemegride and has

somewhat more potent activity than diazepam against convulsion induced by pentylenetetrazol and convulsion of El strain mice, but was less potent than diazepam against convulsions induced by strychnine and electroshock. On the impairment of motor function, CS-370 is definitely less effective than diazepam. On the emesis produced by apomorphine hydrochloride in dogs and tremorine induced symptoms in mice, CS-370 is not significantly inhibitory. CS-370 belongs to the same group of minor tranquilizers as diazepam. It was found that CS-370 is characterized by low toxicity and minimal adverse side-effects.

174760 Bopp, Barbara; Biel, John H. Division of Experimental Therapy, Abbott Laboratories, North Chicago, IL 60064 **Antidepressant drugs.** Life Sciences (Oxford). 14(3):415-423, 1974.

Certain structure - activity relationships were identified among the tricyclic antidepressants, especially for the pharmacologic activity. The secondary amines are more potent inhibitors of norepinephrine uptake while the tertiary amines are more potent inhibitors of serotonin uptake. Clinically, the structure - activity relationships are less clear. Current theories suggest that the secondary amines have predominantly stimulant properties and tend to increase levels of psychomotor activation and drive, suggesting a possible correlation with activity in noradrenergic neuronal systems. In contrast, tertiary amines have predominantly mood elevating properties and/or sedative, antianxiety effects, suggesting a possible correlation with activity in serotonergic neuronal systems. 12 references. (Author abstract)

174764 Chiel, Hillel; Yehuda, Shlomo; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Development of tolerance in rats to the hypothermic effects of d-amphetamine and apomorphine.** Life Sciences (Oxford). 14(3):483-488, 1974.

The development of tolerance in rats to the hypothermic effects of D-amphetamine and apomorphine was discussed. Rats given d-amphetamine or apomorphine and placed in a cold environment developed marked hypothermia. After daily injections of either drug for 7 weeks, the maximal hypothermic responses to d-amphetamine or apomorphine were reduced to 72% and 19% of those obtained initially. Subsequent injection of ET-495, a central dopamine receptor stimulant, caused rectal temperature to decrease only 72% and 49% as much as in control animals. The hypothermic response to apomorphine was also depressed in d-amphetamine treated animals. 7 references. (Author abstract modified)

174828 Crooks, P. A.; Little, Hilary J.; Rees, J. M. H. Dept. of Pharmacy, University of Manchester, Manchester, M13 9PT, United Kingdom **The effects of amphetamine, 2-aminoindane and 2-aminotetralin on the concentrations of whole brain noradrenaline, dopamine, 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in the mouse.** Journal of Pharmacy and Pharmacology (London). 25(Supplement):124P, 1973.

Mice were injected with amphetamine, 2-aminoindane, and 2-aminotetralin in order to determine their effects on the concentrations of whole brain noradrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA). Fifteen minutes after amphetamine injection there were no significant changes in any of the amines but there was a significant reduction in NA and DA. Fifteen minutes after injection of 2-aminoindane the only change was a reduction in 5-HIAA and 120 minutes after injection there was no change in any of the amines. 2-Aminotetralin had similar effects at the earlier time level but at 120 minutes there were significant increases in DA and 5-HT. The results indicate that the central biochemical balance concurrent with maximum antinociceptive action differs from that concurrent with maximum respiratory stimulation. The former is associated with changes in 5-HIAA, the latter with changes in DA and/or NA. 2 references.

174877 Deutsch, Robert. Department of Psychology, Atkinson College, York University, 4700 Keele Street, Downsview M3J2R7, Ontario, Canada **Conditioned hypoglycemia: a mechanism for saccharin-induced sensitivity to insulin in the rat.** Journal of Comparative and Physiological Psychology. 86(2):350-358, 1974.

The reliability of the finding that ingestion of saccharin potentiates insulin induced mortality was evaluated and a number of predictions of the conditioned hypoglycemia account of this effect were tested. Saccharin ingestion was found to potentiate insulin induced mortality and this potentiating effect is accounted for by the hypothesis that the taste of saccharin elicits hypoglycemia as a conditioned response. It is shown that saccharin ingestion alone produces

hypoglycemia in the same experimental context. As predicted by the conditioning hypothesis, long-term access to saccharin was found to extinguish the hypoglycemic response. Further experiments showed that the hypoglycemic response can be elicited by stimuli, either gustatory or olfactory, which are paired with intragastric glucose administration. These results support the conditioning account of the potentiating effect of saccharin on insulin induced mortality and suggest that hypoglycemia occurs as a conditioned response in anticipation of feeding. 27 references. (Author abstract modified)

174959 Taylor, William Allan. Vanderbilt University, Nashville, TN **Effects of amphetamine and its hydroxylated metabolites on central noradrenergic mechanisms. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-1632 HC$10.00 MF$4.00 171 p.

The effects of the optical isomers of amphetamine and hydroxylated metabolites on the central noradrenergic system were studied following their intraventricular administration. Both dextro and l-amphetamine produced motor stimulation, as did p-hydroxynorephedrine. The optical isomers of p-hydroxyamphetamine produced profound locomotor stimulation. The intraventricular administration of both isomers of amphetamine had no effect on cerebral norepinephrine. All the optical isomers of amphetamine and its hydroxylated metabolites did not block the initial accumulation of radioactivity or the uptake of H3-normetanephrine and a decrease in that of the deaminated catechol metabolites. d-Amphetamine, and to a lesser extent l-amphetamine, increased the turnover rate of brain norepinephrine. The hydroxylated metabolites decreased the turnover of brain norepinephrine. The data emphasize the complexity of the pharmacology of amphetamine and clarify the role of its para-hydroxylated and beta-hydroxylated metabolites in its pharmacological and biochemical profile. Hydroxylated metabolites appear involved in the metabolic regulation of central norepinephrine containing neurons. (Journal abstract modified)

174960 Van Tyle, William Kent. Ohio State University, Columbus, OH **Pharmacokinetic disposition of norapomorphine derivatives and its influence on the elicitation of stereotypical gnawing. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-2150 HC$10.00 MF$4.00 141 p.

Fluorometric assay procedures developed for three N-substituted norapomorphine derivatives were employed to determine the disposition patterns of the compounds in the brain and the whole bodies of mice. The compounds were norapomorphine, apomorphine, and N-n-propyl-norapomorphine. Apomorphine and the n-proply derivative attained peak brain concentrations in mice within 1 min after intravenous administration. Both compounds disappeared from brain and whole animal by a biphasic, first order process characterized by an initially rapid disappearance phase followed by a slower phase. The peak brain concentration of norapomorphine was reached 5 to 10 min after intravenous administration. Norapomorphine disappeared from the brain at a slower rate than from the whole animal, suggesting that the compound may be preferentially retained by nervous tissue. The median effective brain concentration required to produce stereotyped gnawing was determined for the three compounds and relative potency determinations were made. Norapomorphine was least potent, and apomorphine was most potent. (Journal abstract modified)

174962 Reigle, Thomas George. Ohio State University, Columbus, OH **Potential neurotransmitters and receptor mechanisms involved in the central control of body temperature in hamsters. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-2106 HC$10.00 MF$4.00 253 p.

The consequences of the central administration of biogenic amines on temperature regulation were studied in hamsters. The hamsters were stereotaxically implanted with permanent brain cannulae in the anterior hypothalamic-preoptic area. The experiments were conducted at an ambient temperature of 20 degrees C. The exposure of hamsters to a cold environment resulted in the initiation of shivering, peripheral vasoconstriction and increased cardiac rate. Continued heat exposure elicited decreased skeletal muscle activity and heartrate in conjunction with peripheral vasodilation. Centrally administered l-norepinephrine (NE) bitartrate produced a dose dependent decrease in rectal temperature and heartrate accompanied by a decrease in electromyographic activity and an increase in foot skin temperature. Peripherally effective doses of receptor antagonists were injected into the same hypothalamic site 1 hour before NE completely abolished the response or left it unaltered. Car-

bamylcholine (CCh) chloride elicited a dose related increase in rectal temperature. A higher dose produced marked behavioral arousal and a decrease in rectal temperature. Atropine injected into the same site 1 hour prior to the administration of CCh eliminated the effects. Centrally administered serotonin had no influence on temperature regulation. (Journal abstract modified)

174963 Freeman, John Jay. Vanderbilt University, Nashville, TN **Amphetamine-tricyclic interactions: role of the hydroxylation of amphetamine in its central and peripheral mode of action. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-1615 HC$10.00 MF$4.00 167 p.

The mechanism by which iprindole enhances the central stimulatory effect of amphetamine was studied in rats. The role of the hydroxylated metabolites of amphetamine, p-hydroxyamphetamine, and p-hydroxynorephedrine in the central and peripheral mode of action of amphetamine were also examined. The potentiation of the central action of amphetamine by iprindole resulted mainly from inhibition of the hydroxylation of amphetamine. A blockade of the nueronal membrane pump for catecholamines was not a requirement for the antidepressant effect of tricyclics. The results obtained with iprindole and amphetamine supported the view that amphetamine is pharmacologically active as the parent compound in both the peripheral and central nervous system. The hydroxylated metabolites of amphetamine were not essential for the initial reduction of catecholamines elicited by amphetamine. The maintenance of depletion, both centrally and peripherally was, however, associated with the formation and accumulation of p-hydroxynorephedrine in tissue. Iprindole was a more viable tool than the classical tricyclics to study biochemical mechanisms of action of amphetamine. (Journal abstract modified)

174964 Milzoff, Joel Robert. Indiana University, Bloomington, IN **Cardiovascular pharmacology of delta9-tetrahydrocannabinol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-2736 HC$10.00 MF$4.00 143 p.

The cardiovascular and respiratory rate effects of intravenously administered, 99% pure delta9-tetrahydrocannabinol (THC) were studied with the solvent system of bovine albumin in Harlan Wistar rats. Depression of heartrate was seen to be the result of a nondirect action on the heart. The changes in heartrate, blood pressure, and internal body temperature appear to result from an interaction between THC and the central nervous system, specifically, of the hypothalamus, although the possibility of some degree of peripheral cholinergic involvement exists. (Journal abstract modified)

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167324 Hooghe-Peters, Elisabeth L. Faculte des Sciences Psychologiques et Pedagogiques, Universite Libre de Bruxelles, 2, Evers St., B-1000 Brussels, Belgium **Effect of L-asparaginase on retention of maze learning in mice.** Life Sciences Oxford. 13(3):185-190, 1973.

The effect of L-asparaginase on retention of maze learning in rats was investigated by injecting the enzyme into mice by an intrathecal or by an intraperitoneal route. The result was a significant impairment of memory. Glutamine and asparagine prevented the effect of asparaginase when injected by the interperitoneal route. 21 references. (Author abstract modified)

167362 Alves, Claudio Norberto; Carlini, Elisaldo Araujo. Universidade Federal Rural de Pernambuco, Instituto de Ciencias Biologicas, Pernambuco, Brazil **Effects of acute and chronic administration of Cannabis sativa extract on the mouse-killing behavior of rats.** Life Sciences (Oxford). 13(1):75-85, 1973.

The effects of acute and chronic administration of Cannabis sativa extract on mouse killing behavior was studied in rats. The muricidal behavior of spontaneous killer rats was blocked after the first injection of cannabis while nonkiller rats became killers after the 10th injection. The effect was potentiated by starvation which by itself did not interfere with the behavior of the nonkiller rats. Suppression of muricidal behavior may occur due to the acute depressant effects of marihuana. Under chronic administration tolerance develops to these effects unmasking hyperemotionality and/or irritability which may induce killing behavior in previously nonkiller rats. 32 references. (Author abstract modified)

167398 Vardaris, Richard M.; Gaebelein, Claude; Riccio, David C. Kent State University, Kent, OH 44242 **Retrograde amnesia from hypothermia-induced brain seizures.** Physiological Psychology. 1(3):204-208, 1973.

In two experiments using male rats of the Sprague-Dawley strain, hypothermia produced retrograde amnesia (RA) for passive avoidance and induced paroxysmal spike discharges in cortical EEG. These findings suggest that the cessation or even diminution of electrical activity in the CNS is probably not a necessary condition for obtaining RA after deep body cooling. Weak doses of strychnine had no apparent effect on behavior but hastened onset of brain seizures during cooling. It is concluded that while hypothermia and ESB are qualitatively different treatments, they both may produce RA through a common mechanism -- disruption of normal brain activity by bursts of seizure like spike activity. 15 references. (Author abstract modified)

167401 Worsham, Elizabeth; Hamilton, Leonard W. Department of Psychology, Rutgers University, New Brunswick, NJ 08903 **Acquisition and retention of avoidance behaviors following septal lesions or scopolamine injections in rats.** Physiological Psychology. 1(3):219-226, 1973.

A study was made of 41 male albino rats (CFE strain) to report on the acquisition and retention of avoidance behaviors following septal lesions or scopolamine injections. Scopolamine injections and septal lesions were found to have similar behavioral effects on both the acquisition and retention of a two way avoidance task. Scopolamine impaired the acquisition of a jump up avoidance such that the animals did not even learn the response, whereas septal lesions resulted in no change in acquisition of this task. Septal lesions prior to retention testing resulted in significantly shorter latencies to jump, but scopolamine injections were found to impair retention of this task. These results were interpreted to support the hypothesis that multiple functional systems may be represented within the septum. It is recommended that additional studies involving more selective lesions and different drugs are necessary to determine more precisely the nature of behavioral inhibition. 41 references. (Journal abstract modified)

167403 Gattoni, Renata C.; Izquierdo, Ivan. Departamento de Farmacologia, Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Estafeta 32, Cordoba, Argentina **Effect of chronic posttrial saline injections on maze performance.** Physiological Psychology. 1(3):231-232, 1973.

Twenty adult albino rats (Wistar) were used to study the effect of chronic posttrial saline injections on maze performance. Chronic posttrial IP injections disrupt the performance of rats in a Lashley III maze for a wet food mash as a reward after 20 sessions. In addition, the treatment causes several signs of emotional disturbance: increases latency to leave the startbox, squealing, defecation, and urination. These effects are attributable to aversive properties of the injection procedure, and these results should be considered as a cautionary note to those who study the effect of chronic posttrial drug injections on learning. 9 references. (Journal abstract modified)

167813 Sieroslawska, Janina; Hano, Jozef. Dept. of Pharmacodynamics, Medical Academy, Krakow, Poland. **In the search for new tranquillizing drugs.** Materia Medica Polona (Warsaw). 4(1):3-8, 1972

Three derivaties of gamma-butyrolactone: gamma-methyl-gamma-butyrolactone (MBL), alpha-(p-aminophenyl)-gamma-methyl-gamma-butyrolactone (LC), and alpha-(p-dimethylaminophenyl)-alpha-allyl-gamma-methyl-gamma-butyrolac one (LP) were examined by behavioral methods. All three compounds produced tranquilizing effects in mice, rats, pigeons and cats; the least active was MBL. In some tests LC exerted stimulatory or antidepressive effects. LC and LP compounds show advantageous efficiency coefficient and, unlike unsubstituted gamma-butyrolactone, do not posses hypnosedative properties. 48 references. (Author abstract modified)

168230 Greenberg, Isaac. Syracuse University **The effects of L-(delta)-9-trans-tetrahydrocannabinol on low and high response rates generated under two similar conditions (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-19814 HC$10.00 MF$4.00 131 p.

Experiments were conducted to determine the generality of the depressive and sedative effects of L-delta9-trans-tetrahydrocannabinol (THC) in rats and to define the relevant variables determining such effects. Experiment one examined the influence of THC on responding generated under 2 min. or 4 min. fixed-interval contingency, demonstrating that the drug had little effect in the normally low rate early portion of the interval, but significantly suppressed rates in the later, high rate, stages. Experiment two also examined the influence of THC on both high and low response rates, in the condition where rates were controlled

by external stimuli which signalled either the presence or absence of food availability. While low rates remained unchanged, high response outputs, generated when food was available, were greatly attenuated following THC administration. The properties of THC, along with some of its other characteristics, are discussed with the aim of classifying THC as similar to, but not identical with, the barbiturates and narcotic analgesics. (Journal abstract modified)

168438 Tilson, H. A.; Sparber, S. B. Department of Pharmacology, Michigan State University, East Lansing, MI 48823 **The effects of d- and l-amphetamine on fixed-interval and fixed-ratio behavior in tolerant and nontolerant rats.** Journal of Pharmacology and Experimental Therapeutics. 187(2):372-379, 1973.

Male, albino rats were trained to press a lever for food pellets on a fixed-interval (FI) 75 second or a fixed-ratio (FR) 30 schedule of reinforcement. The dose related effects of d- or l-amphetamine on responding during successive 15 second segments of the FI 75 second interval, as well as the overall response rate, were investigated. The lack of a complete cross-tolerance using either schedule of reinforcement suggests that d- and l-amphetamine are producing unequal peripheral and/or central effects at the doses employed, and therefore may be affecting the schedule controlled behavior by different mechanisms of action. Further investigations are needed to identify the pharmacodynamic changes after repeated administration of the amphetamines and their possible interaction with the phenomenon of behavioral tolerance. 25 references. (Author abstract modified)

168439 Holtzman, Stephen G.; Jewett, Robert E. Emory University, Department of Pharmacology, Atlanta, GA 30322 **Stimulation of behavior in the rat by cyclazocine: effects of naloxone.** Journal of Pharmacology and Experimental Therapeutics. 187(2):380-390, 1973.

The actions of cyclazocine, a potent analgesic with mixed agonist and narcotic antagonist properties, were evaluated on two distinct types of behavior in the rat: lever pressing maintained under a continuous avoidance schedule and locomotor activity. The effects of cyclazocine on the total brain content of norepinephrine, dopamine and serotonin were also examined. Dose response curves were determined for cyclazocine alone, then redetermined with concomitant administration of naloxone at two dose levels. d-Amphetamine was also tested alone and with naloxone on avoidance behavior. Cyclazocine increased avoidance responding and locomotor activity in a graded manner over a broad range of doses. Both behaviors were disrupted by the highest doses of cyclazocine. The findings were consistent with the view that the agonistic component of action of some narcotic antagonists is mediated by several mechanisms, at least one of which is not blocked by naloxone. The interaction between naloxone and d-amphetamine emphasized the need for further evaluation of possible interactions between narcotic antagonists and psychoactive drugs of classes other than the opioid. 38 references. (Author abstract modified)

168718 Lovecky, Deirdre V.; Dewsbury, Donald A. University of Florida, Gainesville, FL 32601 **Effects of imipramine on copulatory behavior of male rats.** Bulletin of the Psychonomic Society. 2(4):237-239, 1973.

Each of 16 male rats completed three tests of copulatory behavior: following saline injection and two different dosages of imipramine. Imipramine produced a prolongation of the intervals between intromissions within series and of the intervals between ejaculation and the resumption of copulation for all series tested. The number of intromissions required to attain ejaculation was reduced in all series. The effects are interpreted in the context of data relating male and female copulatory behavior to brain monoaminergic function. 21 references. (Author abstract)

168833 McKim, W. A. Dept. of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **The effects of scopolamine on fixed-interval behaviour in the rat: a rate-dependency effect.** Psychopharmacologia (Berlin). 32(3):255-264, 1973.

The effects of scopolamine on fixed-interval behavior was examined in the rat. Eight rats trained on a fixed-interval of 2 min. for food reinforcement were injected with scopolamine hydrobromide at 3.2mg/kg on a number of sessions. The drug increased responding that was normally slow early in each interval and decreased high rates of responding normally seen near the end of each interval. It was concluded that scopolamine has a rate dependent effect similar to amphetamine and other drugs. 35 references. (Author abstract modified)

168834 Ridgers, Andrew; Gray, Jeffrey A. Univ. of Oxford, Dept. of Experimental Psychology, South Parks Rd., Oxford OX1 3PS, England **Influence of amylobarbitone on operant depression and elation effects in the rat.** Psychopharmacologia (Berlin). 32(3):265-270, 1973.

The influence of amylobarbitone on operant depression and elation effects was examined in the rat. In a daily session, reward was given for barpressing on a variable interval schedule; on odd days it consisted of 1 pellet and on even days of 4 pellets. The low and high reward schedules were each associated with discriminative stimuli (SD). During each session the schedule and associated SD changed for two brief intrusion periods to the ones opposite to that day's baseline conditions. Response rates were significantly lower during the low reward intrusion periods than when low reward was the baseline and significantly higher during the high reward intrusion periods than when high reward was the baseline. The response rate differences appear to constitute within S operant analogues of the Crespi depression and elation effects, respectively, observed in runways. The operant depression effect was reduced by amylobarbitone sodium but the elation effect was unaffected supporting the view that amylobarbitone impairs behavioral responses to departures from expected magnitude of reward only when the departure is in an unfavorable direction. 6 references. (Author abstract modified)

168835 Lorens, Stanley A.; Mitchell, Clifford L. Institute of Physiology, Univ. of Bergen, Arstadveien 19, N-5000 Bergen, Norway **Influence of morphine on lateral hypothalamic self-stimulation in the rat.** Psychopharmacologia (Berlin). 32(3):271-277, 1973.

A study of the influence of morphine on the lateral hypothalamic self-stimulation in the rat was presented. Morphine both suppressed and elevated lateral hypothalamic self-stimulation response output. The duration of the depressant effect and the temporal appearance of the excitatory influence were dose dependent. With repeated daily injection, tolerance developed to the suppressive effect while the facilitatory effect appeared earlier and tended to be enhanced. Thus the facilitatory action is not due to a rebound phenomenon. No correlation between the effects of morphine on self-stimulation behavior and on wheel running activity was observed. 6 references. (Author abstract)

168837 Glow, Peter H.; Russell, Alan. Dept. of Psychology, Univ. of Adelaide, Adelaide, South Australia 5001 **Drug enhanced sensory contingent bar pressing: comparing the effect of contingent and noncontingent sensory change.** Psychopharmacologia (Berlin). 32(3):285-292, 1973.

The possible mechanisms underlying the enhanced responding to bar pressing for sensory change as the reinforcer by the administration of dexamphetamine (DA) or a mixture of DA and amylobarbitone and the effects of response contingent (feedback) vs noncontingent sensory change on responding under the two drugs separately, their mixture, or placebo were investigated. Phase I animals were reinforced with a light and sound change combined and given drug injections prior to each of 18 20 min. trials. In Phase II, the four drug treatments were each divided into seven matched groups operating under different reinforcement conditions to assess: the effect of deleting either the sound or light component of the reinforcer; and the effect of giving the deleted change or changes on a noncontingent basis. Responding declined when either the sound or both the sound and light were deleted but was not affected by the presence of noncontingent sensory change. It was concluded that DA and the mixture operate directly to enhance the reward value of feedback sensory change. 10 references. (Author abstract modified)

168838 Milhaud, C.; Klein, M.; Chapouthier, G. Service de Neurophysiologie, Centre de Recherches de Medecine Aeronautique, 5 bis, Avenue de la Porte de Sevres, 75015 Paris, France **/The social play behavior of chimpanzees according to a psychopharmacological test/.** Le comportement social de jeu des chimpanzes en tant que test psychopharmacologique. Psychopharmacologia (Berlin). 32(3):293-300, 1973.

The action of diazepam on the social play behavior of a stable group of four chimpanzees was studied. Results revealed the tranquillizing effect of the drug in doses as low as 1 mg/kg orally. A reduction in solitary activities, an increase in interactions with the observers and an increase in vocalization by the animals was seen. Diazepam was shown to exert a specific action dependent on the particular behavioral type of each animal. 10 references. (Author abstract)

169028 Wilson, Marvin C. no address **Psychomotor stimulant self-administration in the rat.** Final Report, NIMH Grant MH-21618, 1973. 15 p.

The applicability of using data generated from rat self-administration studies to predict the potential abuse liability of compounds possessing pharmacological profiles similar to psychomotor stimulants was investigated. The basic procedure consisted of conditioning rats to self-administer intravenously a saline solution of cocaine hydrochloride. Following stabilization, various doses of the compounds were substituted for the cocaine solution. It was found that: 1) initiation of the behavior without using other contingencies is difficult; 2) unit dosages of cocaine previously reported as reinforcing, produce an increase in locomotor activity which may be associated with the reinforcing actions of the compound or its self-administration; 3) the chronic administration of cocaine, even at low doses at 3 day intervals is debilitating in the rat; 4) chronic indwelling jugular cannulae remain viable up to 4-6 weeks only; 5) most Ss exposed noncontingently to infusions of cocaine at doses and rates previously reported as reinforcing do not find it reinforcing; and 6) cocaine self-administration behavior can be initiated and maintained at a stable daily rate when drug access time is limited to 1-2 hr in a minority of Ss. (Author abstract modified)

169469 Dupeyron, J. P.; Boulu, R.; Rossignol, P. Universite Rene Descartes, 4 Avenue de l Observatoire 7006 Paris, France **/Evaluation of central antireserpine effect by the use of light blink reflex./** Mise en evidence et mesure d'une activite antireserpine au niveau central au moyen du reflexe de clignement a la lumiere. Psychopharmacologia (Berlin). 33(1):87-94, 1973.

Central antireserpine effect was evaluated by the use of the light blink reflex. Psychotropic drugs (tricyclic antidepressant agents, amphetamine, chlorpromazine, chlorprothixene) were administered by slow intravenous infusion to reserpinized rabbits until the blink reflex had disappeared. The proposed method does not display particular specificity but is suitable for measurement of antireserpine activity at the central level. 19 references. (Author abstract modified)

169473 Blozovski, D.; Blozovski, M. Universite Paris VI, 4 place Jussieu, 75230 Paris Cedex 05, France **/Effects of atropine on exploration, learning and electrocortical activity in the developing rat./** Effets de l'atropine sur l'exploration, l'apprentissage et l'activite electrocorticale chez le Rat au cours du developpement. Psychopharmacologia (Berlin). 33(1):39-52, 1973.

The effects of atropine on exploration, learning and electrocortical activity were studied in the developing rat. With 10mg/kg, adult rats exhibited disordered hyperactivity and enhanced exploratory behavior; this effect was not seen with 2.5mg/kg. Younger rats became drowsy and showed lower exploratory activity even with smaller doses; the dose of 0.1mg/kg was ineffective. Retention of recent learning was entirely blocked in the youngest, weakly impaired in the 23-day-old and not influenced at all in older rats. In all age groups, atropine induced slower EEG activity. The results are consistent with the hypothesis of a double reticulolimbic system modulating arousal, and with the caudal rostral sequence of development of these systems in the rat. 39 references. (Author abstract modified)

170126 Kostowski, W.; Czlonkowski, A. Department of Experimental Pharmacology, Medical Academy of Warsaw, Krakowskie Przedmiescie 26/28,00 927 Warsaw, Poland **The activity of some neuroleptic drugs and amphetamine in normal and isolated rats.** Pharmacology 10(2):82-87, 1973.

The effects of some neuroleptic drugs and amphetamine on the mouse killing behavior of Wistar male rats exposed to prolonged isolation or maintained in groups were investigated. Isolation induced mouse killing attitudes in about 60% of the rats. Isolated rats were less reactive to cataleptogenic doses of neuroleptics, such as chlorpromazine and haloperidol and more sensitive to amphetamine than grouped animals. Differences were also noted in reactivity to drugs between killers and isolated nonkillers. 22 references. (Author abstract)

170162 Dubinsky, Barry; Karpowicz, J. Krystyna; Goldberg, Morton E. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Effects of tricyclic antidepressants on attack elicited by hypothalamic stimulation: relation to brain biogenic amines.** Journal of Pharmacology and Experimental Therapeutics. 187(3):550-557, 1973.

Stimulus bound attack attenuating activities of chlorimipramine (CMI), imipramine (IMI) and desipramine (DSI) were compared in cats having chronically implanted hypothalamic electrodes. The ED50 values of IMI and CMI were 8.5and 3.4mg/kg, respectively; and CMI as 2.5times as active as IMI. DSI at a dose of 12mg/kg affected only three of six Ss. The possible mechanism by which CMI may have exerted its effects was ex-

plored in other Ss. The minimum effective attack blocking dose of CMI was established and they received CMI 1 day after and at intervals of 1, 2.5, and 5 weeks after p-chlorophenylalanine methyl ester HCl treatment (PCPA). PCPA alone did not alter the pattern of attack, but the minimum effective attack blocking dose of CMI was no longer effective after PCPA. The attack blocking effects of CMI reappeared after its repeated administration, 2.5to 5 weeks after PCPA. Doses of 5-hydroxytryptophan which were devoid of effects on attack when administered alone, temporarily restored the inhibitory effects of CMI in PCPA treated Ss. In another group, 6 hydroxydopamine treatment did not appreciably alter the attack blocking properties of CMI, and lowered hypothalamic norepinephrine (NE). The possible mechanisms of action of CMI in aggressive behavior appears related to an interaction with brain 5-hydroxytryptamine, rather than to brain NE. 28 references. (Author abstract modified)

170177 Kruk, Z. L. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, London E1 2AD, England **Dopamine and 5-hydroxytryptamine inhibit feeding in rats.** Nature: New Biology (London). 246(150):52-53, 1973.

An investigation of the neurotransmitters involved in mediating anorectic responses in rats was described. Rats were injected i.p. with either d-amphetamine or desethylfenfluramine 30 m before presentation of food and following pretreatments with saline, pimozide or cyproheptadine. Pimozide antagonized the anorectic activity of d-amphetamine and the anorexia due to desethylfenfluramine was antagonized by cyproheptadine. Injections of d-amphetamine, dopamine and the anorexia due to desethylfenfluramine was antagonized by cyproheptadine. Injections of d-amphetamine, dopamine and apomorphine i.c. caused a dose dependent decrease in the food eaten in the first hour after presentation. Their anoretic effect was abolished following pretreatment with pimozide 2 h previously. It was suggested that d-amphetamine anorexia is mediated by activation of dopaminergic mechanisms and desethylfenfluramine anorexia is mediated by activation of 5-hydroxytryptamine mechanisms. 10 references.

171259 Park, Chan Woong; Chang, Hyoun Kab; Cho, Hang Young. Department of Pharmacology, Seoul National University, Seoul, Korea **Effects of chlorpromazine, meprobamate and chlordiazepoxide on the maze learning in mice.** Korean Central Journal of Medicine (Seoul). 22(4):435-440, 1972.

In order to assess the effect of tranquilizers on maze learning, mice were tested in a single water T-maze after one of the following drug treatments: physiological saline; 1.25mg/kg of chlorpromazine; 20mg/kg of meprobamate; and 10mg/kg of chlordiazepoxide. The test apparatus was a galvanized steel T-tank 11.5cm wide and 18 cm deep. The maze was filled with 22-24 degree C water to a depth of 10 cm. Drugs were administered intraperitoneally 20-30min. before testing. A session consisted of 3 adaptation and 20 consecutive test trials. The number of correct trials and swimming speed were used as an index of learning performances. It was found that, as compared to physiological saline, the number of correct trials were significantly decreased and the swimming speed was significantly delayed after administration of chlorpromazine, but the number of successful trials and swimming time were not changed significantly after administration of meprobamate and chlordiazepoxide. 24 references. (Journal abstract)

171300 Puri, Surendra K.; Lal, Harbans. College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Effect of dopaminergic stimulation or blockade on morphine-withdrawal aggression.** Psychopharmacologia (Berlin). 32(2):113-120, 1973.

Aggregation during morphine abstinence elicited social aggression (rearing, vocalization, attack bites) in the morphine dependent rats. Pretreatment with L-dihydroxyphenylalanine DL-dihydroxyphenylalanine, dextro-amphetamine sulfate or apomorphine hydrochloride enhanced that aggression several fold. Alpha methyl-p-tyrosine abolished the morphine withdrawal aggression that was elicited either by mere aggregation or by aggregation combined with amphetamine. However, alpha methyl-p-tyrosine did not block the aggression in apomorphine treated rats. Haloperidol also blocked the aggression due to mere abstinence or abstinence supersensitized by amphetamine. Similarly, methadone hydrochloride blocked morphine withdrawal aggression supersensitized by apomorphine. These data are interpreted to suggest dopaminergic basis of morphine withdrawal aggression and a latent supersensitivity of dopaminergic neuropathways during morphine dependence. 26 references. (Author abstract modified)

171302 Houser, Vincent P.; Houser, Frances L. Veterans Administration Hospital, Perry Point, MD 21902 **The effects of agents that modify muscarinic tone upon behavior controlled by an avoidance schedule that employs signaled unavoidable shock.** Psychopharmacologia (Berlin). 32(2):133-150, 1973.

Six male squirrel monkeys were subjected to a Sidman nondiscriminated avoidance schedule that superimposed conditioned stimuli (CS) -- unavoidable shock pairings -- upon the ongoing avoidance behavior. Four of the six animals demonstrated facilitated avoidance response rates during the CS, while two demonstrated suppressed rates during the CS. Scopolamine hydrobromide reversed these patterns, causing the facilitators to suppress and vice versa. Scopolamine hydrobromide also led to a reliable reduction in overall response rate and an increase in the number of shocks received. Neither scopolamine methylbromide, a peripheral acting anticholinergic, nor pilocarpine nitrate, a muscarinic stimulant, produced any reliable effects upon avoidance behavior. These results were interpreted to indicate that the central acting antimuscarinic agent, scopolamine hydrobromide, may be able to reduce level of fear motivation either directly by interfering with cholinergic systems that mediate fear or by producing decrements in cognitive processes that are needed for animals to fully appreciate the aversive qualities of the CS. 25 references. (Author abstract)

171304 Robichaud, R. C.; Sledge, K. L.; Hefner, M. A.; Goldberg, M. E. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Propranolol and chlordiazepoxide on experimentally induced conflict and shuttle box performance in rodents.** Psychopharmacologia (Berlin). 32(2):157-160, 1973.

Propranolol failed to attenuate the suppression of behavior caused by experimentally induced conflict in rats and failed to enhance the avoidance performance of partially trained mice in a shuttle-box situation, effects which are observed after chlordiazepoxide. When given in combination with chlordiazepoxide, propranolol did not influence the effects of the tranquilizer in either procedure. 11 references. (Author abstract)

171306 Drew, W. G.; Miller, Loren L.; Baugh, E. L. Department of Psychiatry, University of Kentucky, College of Medicine, Lexington, KY 40506 **Effects of delta9-THC, LSD-25 and scopolamine on continuous, spontaneous alternation in the Y-maze.** Psychopharmacologia (Berlin). 32(2):171-182, 1973.

The effects of delta9-THC, LSD-25 and scopolamine on continuous, spontaneous alternation of the hooded rat in the Y-maze were determined. LSD and scopolamine decreased the number of arm entries (responsivity) while concomitantly reducing percent alternation. THC however, reduced responsivity and percent alternation more at the lower dose (1 mg/kg) when compared to control than at the higher dose (3 mg/kg). Only scopolamine induced a significant increase in stimulus perseveration. The results are discussed in relation to the advantages afforded by the continuous spontaneous alternation procedure. 18 references. (Author abstract)

171308 File, Sandra E. Department of Psychology, City of London Polytechnic, London, England **Interaction between prior experience and the effects of chlorpromazine on exploration in the rat.** Psychopharmacologia (Berlin). 32(2):193-200, 1973.

In a study to determine interaction between prior experience and the effects of chlorpromazine on exploration in rats, 4 mg/kg chlorpromazine increased the latency to start exploring a new environment, and decreased the time spent exploring it and novel objects in it. A prior, undrugged experience of the apparatus reduced this drug effect, whereas a prior, drugged experience had little effect on later exploration under saline conditions. Rats placed undrugged in the apparatus on two trials showed significant habituation of exploration, but rats given both trials when drugged did not. 14 references. (Author abstract)

171521 Wolthuis, O. L.; Kepner, Larry A.; Vanwersch, R. A. P. Medical Biological Laboratory TNO, 139 Lange Kleiweg, Rijswijk, The Netherlands **A rapid automatic method for determining shock sensitivities of mice.** Physiology & Behavior. 11(4):447-453, 1973.

An instrumental technique is described which permits rapid blind determination of shock sensitivities of inbred mice. The measured parameter of shock sensitivity was not affected by increased activity of the Ss. Morphine was found to decrease shock sensitivity as a function of dose. 12 references. (Author abstract)

171599 Oh, J. S.; Hong, S. A.; Park, C. W.; Rho, K. S. Dept. of Pharmacology, College of Medicine, Seoul National Univ., Seoul, Korea **The effect of Panax Ginseng saponin on the central nervous system in rat: the psychopharmacological effect of Ginseng.** Seoul Journal of Medicine (Seoul). 14(1):15-18, 1973.

The effects of Panax Ginseng saponin fraction on the rat nervous system was studied through general behavior, open field exploratory behavior and conditioned avoidance behavior. The general behavior of the rat in the home cage was not influenced by 2.5mg/kg of Ginseng saponin fraction but 10mg/kg suppressed general activity. Open field activity was increased by injection of 2.5mg/kg and 5mg/kg of Ginseng saponin fraction compared with control group. Chlorpromazine suppressed conditioned avoidance behavior in the rat but the Ginseng saponin fraction stimulated it. Results suggest that Panax Ginseng fraction has a protective adaptogenic action. 13 references. (Journal abstract modified)

171607 Christensen, A. V.; Pedersen, V. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, 7-9 Ottiliavej, DK 2500 Copenhagen-Valby, Denmark **The effect of pipradrol in mice and its antagonism by neuroleptic drugs.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):8, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the behavioral effect of pipradrol in mice was examined and compared with that induced by methylphenidate. The gnaw compulsion syndrome was studied in mice pretreated with the tyrosine hydroxylase inhibitor H 44/68. H 44/68 completely abolished the compulsive gnawing. L-DOPA 1 h before testing reactivated the mice pretreated with H 44/68. It was shown that pretreatment with the dopamine-beta-hydroxylase inhibitor 4 and 1 h's before hardly affected the compulsive gnawing. A complete inhibition of the excitatory effects of pipradrol was obtained by pretreatment with reserpine 20 h before pipradrol. A number of neuroleptics were tested for antagonistic effect and it was found that the clinically very potent neuroleptics also were most potent with respect to pipradrol antagonistic effect. The methyl-phenidate antagonism test yielded a better differentiation between the weaker basal neuroleptics and the very potent ones than does the pipradrol antagonism test. (Author abstract modified)

171608 Franck, K. F. Department of Pharmacology, H. Lundbeck & Co. A/S, DK-2500 Copenhagen, Denmark **Inhibition of mouse-killing behaviour in rats by some thymoleptic drugs.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):10, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of eight tricyclic and two bicyclic thymoleptic drugs in isolated male rats which killed mice within 2 minutes after presentation were reported. Litracene, nortriptyline, protriptyline and desipramine exhibited greater activity than melitracene, amitriptyline, imipramine and chlorimipramine did. The thiophthalane derivative Lu 5-003 was much more effective than the analogous phthalane derivative Lu 3-010. It is suggested that the inhibitory effect may be related to central noradrenalin (NA) potentiation since most of the secondary amines and in particular Lu 5-003 are uptake inhibitors preponderantly acting on NA neurons whereas the tertiary amines are particularly potent blockers of the 5-hydroxytryptamine membrane pump. 2 references. (Author abstract modified)

171609 Lassen, J. Buus. Research Laboratories, A/S Ferrosan, DK-2860, Soeborg, Denmark **Behavioral effect of tricyclic thymoleptics and chlorpheniramine in mice after pretreatment with 5 hydroxytryptophan (5HTP).** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):11, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the behavioral effect of tricyclic thymoleptics and chlorpheniramine in mice after pretreatment with 5-hydroxytryptophan (5HTP) was reported. The results indicate that the behavioral effect of the 5HT membrane blocking drug chlorimipramine in 5HTP treated mice is caused by an increased serotonergic neuronal activity but a dopaminergic link may also be involved. It is suggested that these drugs do not block the central 5HT receptors activated during the abnormal behavior. (Author abstract modified)

171611 Ahlenius, S.; Anden, N.-E.; Engel, J. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Importance of catecholamine release by nerve impulses for free operant behavior.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):13, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of L-3,4-dihydroxyphenylalanine (LeDOPA) on food reinforced lever pressing behavior and on central catecholamine levels after prior depletion of the catecholamine stores by the granula blocker tetrabenazine (TBZ) or by the tyrosine hydroxylase inhibitor alpha-methyltyrosine methylester hydrochloride (H 44/68) was reported. Both after treatment with TBZ and with H 44/68, the lever pressing rate was markedly depressed. The administration of L-DOPA propionic acid (MK 486), an inhibitor of peripheral DOPA decarboxylase failed to counteract the TBZ induced suppression of the lever pressing. The same treatment, however, resulted in a restoration to normal lever pressing behavior in the H 44/68 pretreated rats. The catecholamine receptor stimulators apomorphine plus clonidine failed to antagonize the inhibition produced by TBZ or H 44/68. The results suggest that the food reinforced lever pressing behavior may be dependent on physiological release of catecholamines by nerve impulses and not on mere stimulation of the catecholamine receptors. (Author abstract modified)

171612 Brown, R. M.; Seiden, L. S. Department of Pharmacology, University of Chicago, Chicago, IL 60637 **Interresponse time changes as a function of deprivation and amphetamine administration.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):14, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, interresponse time (IRT) changes as a function of deprivation and amphetamine administration were reported. Both satiation and amphetamine treatments produced a decrease in response rate and for each treatment the IRT class which was sensitive to change was schedule dependent. Within a schedule, amphetamine and water loading produced similar effects on the overall rate of responding but the two treatments resulted in different effects on the IRTs suggesting that the underlying mechanisms which produce the rate change may be different. (Author abstract modified)

171614 Ahlenius, S.; Engel, J.; Eriksson, H.; Sodersten, P. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Effects of tetrabenazine on lordosis behaviour and on brain monoamines in the female rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):19, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the time course of action of tetrabenazine (TBZ), on the lordosis behavior and on brain monoamines in ovariectomized estrogen pretreated rats was reported. The lordosis behavior was observed 5, 15, 30 minutes and 1, 2, 3, 4, 6, 8 and 10 hours after the injection of TBZ. The analysis of brain noradrenaline (NA), dopamine (DA) and 5-hydroxytryptamine (5-HT) was performed on a separate group of animals 5, 15 minutes and 2, 6 and 10 hours after TBZ. The administration of TBZ produced a significant decrease in brain DA only, and an increase in the lordosis quotient, whereas 10mg/kg of TBZ resulted in the same increase in lordosis behavior as 2mg/kg and a significant reduction of brain NA, DA and 5-HT. The data presented show a covariation in time between an increase in lordosis behavior and a decrease in brain DA. (Author abstract modified)

171615 Meyerson, B. J. Department of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Change of estrogen activated behavior by cycloheximide in the female rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):20, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effect of cycloheximide (Cycl) on estradiol benzoate (EB) activated running wheel activity (RW), sexual motivation (SM), and lordosis response (LR) when mounted by a male was reported in mice. At the day of Cycl treatment the response was depressed below preexperimental level. Thereafter RW and SM increased; the maximal response appeared at about the same time as in only EB treated Ss but did not reach the same level. LR was activated by EB followed by progesterone. The results indicate that Cycl modifies estrogen activated behavior patterns. 5 references. (Author abstract modified)

171616 Lindstrom, Leif H.; Meyerson, Bengt J. Department of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Activation of copulatory behavior by pilocarpine and oxotremorine in the female rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):21, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of cholinergic and anticholinergic compounds when given after estradiol benzoate (EB) treatment only in rats were reported. Atropine did not elicit lordotic behavior when given 50 hours after EB. Pilicar-

pine and oxotremorine effectively activated the lordosis response when given 48 hours after EB treatment. A dose response relationship was obtained. The lordosis response was not seen until at least 3 hours had elapsed from the injection of the muscarinic compound. The muscarinic sysmptoms, however, were most obvious within 30 minutes. Analogous experiments performed in adrenal or hypophysectomized EB treated females revealed that pilocarpine and oxotremorine were not effective to elicit the lordotic behavior in the absence of pituitary - adrenal functions hours after EB treatment. It was found, however, that dexamethasone also prevented the induction of the lordosis response by progesterone in EB treated females. 2 references. (Author abstract modified)

171617 Eliasson, Mona; Michanek, Annika; Meyerson, Bengt J. Department of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **A differential inhibitory action of LSD and amphetamine on copulatory behavior in the female rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):22, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects on lordotic behavior of lysergic acid diethylamide (LSD) and amphetamine, given alone or after pretreatment with p-chlorophenylalanine (PCPA) in rats were reported. LSD inhibited the lordosis response. When PCPA was given 5 hrs before LSD the recovery of the response was slower. Amphetamine also depressed the lordosis response. The inhibitory effect of amphetamine was significantly reduced at the 60 min test after pretreatment with PCPA. It is concluded that LSD was reported to stimulate serotonin receptors in a spinal reflex preparation. In contrast to LSD the inhibitory effect of amphetamine seems to be dependent on functionally available serotonin. 3 references. (Author abstract modified)

171618 Malmnas, Carl Olof; Meyerson, Bengt J. Department of Pharmacology, University of Uppsala, Uppsala, Sweden **Monoamines and copulatory activation in the castrated male rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):23, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the effects of neuropharmacological agents on copulatory behavior in the male rat was reported. Pargyline did not produce an inhibitory effect when given alone, nor in combination with the peripheral decarboxylase inhibitor MK 486. 5-Hydroxytryptophan significantly decreased mount percent. l-DOPA increased mount percent while dl-DOPA had no effect. Apomorphine, which probably increases the central nervous dopaminergic tone, significantly increased mount percent. A clearcut inhibitory effect was obtained by the tyrosine hydroxylase inhibitor alpha-methyl-p-tyrosine but no significant effect by the dopamine-beta-hydroxylase inhibitor. Data support the hypothesis that increased central nervous serotoninergic tone inhibits the male copulatory behavior. 1 reference. (Author abstract modified)

171886 Grilly, David M.; Ferraro, Douglas P. Cleveland State University, Cleveland, OH **Effects of delta9-tetrahydrocannabinol on delayed matching-to-sample choice speeds in chimpanzees.** Bulletin of the Psychonomic Society. 2(6B):413-415, 1973.

The effects of delta9-tetrahydrocannabinol (THC) on choice response speeds in chimapanzee short-term recognition memory were assessed in a delayed matching to sample task. Choice speeds were faster on correct than on incorrect trials and were inversely related to delay length. Although THC lowered matching accuracy, it did not affect any aspect of choice speed. These results were interpreted as indicating that the disruption of short-term recognition memory produced by THC reflects changes in acquisition - storage processes rather than in memory retrieval processes. 13 references. (Author abstract)

171905 Reinis, Stanislav. University of Waterloo, Waterloo, Ontario, Canada **Hydroxylamine interferes with the behavioral response to morphine dependence in mice.** Bulletin of the Psychonomic Society. 2(6A):387-389, 1973.

The interference of hydroxylamine in the behavioral response to morphine dependence in mice is reported. Mice were injected daily by morphine sulfate for 22 days, then forced to drink morphine solution for 5 days, and finally injected with 0.5M hydroxylamine hydrochloride intracranially; 48 hours after the injection, they were given the choice between morphine sulfate solution and water. Hydroxylamine injected animals consumed less morphine solution than two control groups. 10 references. (Author abstract)

172374 Abbatiello, Elvera R. College of Pharmacy, St. John's University, Jamaica, NY 11432 **Alteration of maternal behavior in mice following administration of cyproterone acetate.** Journal of Pharmaceutical Sciences. 63(1):152-153, 1974.

The effect of a long acting, progestational, antiandrogenic compound, cyproterone acetate, on maternal behavior of mice was studied. Cyproterone acetate was administered to 50 female mice at randomly selected stages of gestation; 50 mice served as a control group, and 50 mice were given placebo treatment. Maternal behavior at the time of parturition was altered by the compound, resulting in cannibalization of all offspring of treated mothers immediately or shortly after birth. It is concluded that the possibility exists that cyproterone acetate, by altering the hormonal balance of the mother, may cause atypical maternal behavior. 9 references. (Journal abstract modified)

172454 Smith, Stanley G.; Davis, W. Marvin. Dept. of Pharmacology, Univ. of Mississippi, University, MS 38677 **Haloperidol effects on morphine self-administration: testing for pharmacological modification of the primary reinforcement mechanism.** Psychological Record. 23(2):215-221, 1973.

The effects of haloperidol (HP) on the morphine self-administration of rats was examined to test for possible participation of central dopaminergic systems in the morphine reinforcement mechanism. Rats were allowed to acquire morphine self-administration behavior and then were extinquished. Following extinction, pretreatment with saline and various doses of HP were given before a reacquisition test. Reacquisition data indicated that a low dose of HP increased self-administration while higher doses reduced responding. Data from a second experiment using conditioned reinforcement demonstrated that HP did not block the reinforcing action of morphine. Results are discussed in terms of a need to differentiate between reinforcement antagonism and motor impairment. 9 references. (Author abstract modified)

172745 Kilbey, M. Marlyne; Moore, J. Will, Jr.; Hall, Margaret. Department of Psychology, University of Houston 3801 Cullen Blvd., Houston, TX 77004 **Delta9-tetrahydrocannabinol induced inhibition of predatory aggression in the rat.** Psychopharmacologia (Berlin). 31(2):157-166, 1973.

Delta9-tetrahydrocannabinol induced inhibition of predatory aggression in the rat is reported. Increases in the degree of inhibition were obtained with increasing dosages of the drug. Although sex and strain of the subjects varied nonsystematically, inhibition of predatory aggression uniformly was found to be dose related. Readministration of delta9-tetrahydrocannabinol did not effect motor activity measures at dose levels which inhibit aggression. Administration of delta9-tetrahydrocannabinol increased whole brain serotonin, while norepinepherine is largely unaffected, indicating that the antiaggressive effect may be mediated, in part, by serotonergic mechanisms. 46 references. (Author abstract)

172921 Banerjee, U.; Lin, Geh Sooi. Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia **On the mechanism of central action of amphetamine: the role of catecholamines.** Neuropharmacology (Oxford). 12(10): 917-931, 1973.

The effects of amphetamine were studied on the spontaneous motor activity and other behavior in aggregated mice using a modified jiggle cage. Amphetamine alone produced a fairly dose dependent increase in motor activity, excitatory behavior, and mortality, but effects were abolished after pretreatment with alpha-methyl tyrosine (alpha-MT). Temporary L-DOPA treatment preceding amphetamine restored the effects. Multiple dose pretreatments with reserpine and alpha-methyl-meta-tyrosine (alpha-MMT), singly or in combination, somewhat reduced but did not abolish amphetamine effects (at 8 hr) and invariably augmented these at longer intervals (16 hr), especially after combined pretreatments. Chlorpromazine totally suppressed all amphetamine effects, whereas phenoxybenzamine blocked the hyperexcitability, aggressiveness, and mortality, but not spontaneous motor activity. Results are discussed with relevance to possible roles of noradrenaline and dopamine in mediating amphetamine induced behavior in experiments designed for depletion, repletion and blockage of endogenous catecholamines. 77 references. (Author abstract)

173032 Mello, William F.; Schwartzbaum, J. S. Department of Psychology, University of Rochester, Rochester, NY 14627 **Effects of scopolamine upon behavioral reactivity and visually evoked potential to flashes in rats.** Journal of Comparative & Physiological Psychology. 85(3):469-478, 1973.

Averaged visual evoked response (VER) at cortex and behavioral reactivity to photic stimuli were examined following administration of varying dosages of scopolamine, methyl scopolamine, or saline. The pattern of behavioral and electrophysiological results with scopolamine paralleled earlier findings with septal lesions. The drug impaired habituation of behavioral reactivity to flashes and altered VERs in two ways that appeared to relate to the behavioral impairment. It augmented the positive component of the early negative - positive complex and produced a dissociation between the amplitude of the late negative wave of VER and behavioral activity. These effects were viewed in terms of ascending cholinergic arousal processes and interrelationships of arousal and behavioral patterns. 26 references. (Author abstract)

173039 Cairns, Robert B.; Scholz, Susan D. Department of Psychology, University of North Carolina, Chapel Hill, NC 27514 **Fighting in mice: dyadic escalation and what is learned.** Journal of Comparative & Physiological Psychology. 85(3):540-550, 1973.

The role of reciprocal reactivity in the initial elicitation of attack fighting sequences in isolation raised male mice was clarified. Reactivity of the target animal was manipulated by ip injections of chlorpromazine. As dose levels were increased the probability that an attack would evolve in the interaction decreased monotonically. Attack behavior in isolated animals was thus precisely controlled by diminishing the reactive characteristics of their partners and without direct manipulation of the aggressive subjects themselves. Experiment 2 demonstrated that once attacks had been elicited in previously isolated subjects, the behavior was generalized to other conspecific partners irrespective of the reactivity - nonreactivity of the partner. Supplementary experiments confirm the importance of partner reactivity, regardless of the age of isolation. 14 references. (Author abstract)

173078 Chang, Hyoun Kab; Hong, Suk Yung; Moon, Ick Joo. Dept. of Psychiatry, College of General Studies, Seoul National University, Seoul, Korea **Effects of analeptics on maze learning in mice.** Korean Central Journal of Medicine (Seoul). 21(4):327-332, 1971.

In order to assess the effects of analeptics on learning, mice were tested in a single T water maze after one of the following drug treatments: physiological saline; 0.33mg/kg of strychnine; 1mg/kg of d-amphetamine; or 30mg/kg of caffeine. The test chamber was a galvanized steel T tank 11.5cm wide and 18 cm deep described by Latz et al.(1967). The maze was filled with 22 to 24 degree C water to a depth of 10cm. Drugs were administered intraperitoneally 20 to 30 min before testing. A session consisted of three information and 30 test trials. Correct trials and swimming time served as an index of learning performance. It was concluded that: 1) as compared to physiological saline, acquisition was significantly improved after treatments of strychnine, d-amphetamine and caffeine; and 2) swimming speed did not differ significantly from control but tended to slow in strychnine. 27 references. (Journal abstract modified)

173136 Fechter, Laurence David. University of Rochester **Central monoamines and the acoustic startle reaction in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-25806 HC$10.00 MF$4.00 116 p.

Neurochemical agents capable of altering the startle reaction were investigated focusing on central monoamine (CA) systems involved in elaboration of this reaction in stable and nonstable sensory environments in rats. Chemical assays and histochemical fluorescence analyses of administration of these drugs suggest that NA and 5-HT may have opposing roles in elaborating the reaction in nonstable environments. It is clear that enhancement of 5-HT in the reserpinized animal blocked prepulse inhibition and that even the combined treatment of MK-486, pargyline, and 5-HTP grossly altered the extent of prepulse inhibition. That some prepulse inhibition was present in the latter case indicates partial control over startle output under nonstable sensory conditions and suggests that the CAs may be involved in prepulse inhibition. The most likely candidate is NA and not DA, since findings demonstrate that the former CA does alter startle behavior while the latter does not. That prepulse inhibition was markedly reduced in Ss receiving MK-486, pargyline, and 5-HTP may reflect an imbalance between 5-HT and NA. Data suggest that prepulse stimuli normally result in the inhibition of 5-HT neurons and that this inhibition may be mediated by NA. (Journal abstract modified)

173158 Rowe, Thomas Chester. University of South Dakota **Modification of stimulation-bound**

behavior by trifluoperazine and amphetamine in rats. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27529 HC$10.00 MF$4.00 66 p.

The modification of stimulation bound behavior by trifluoperazine and amphetamine was investigated in rats implanted with stimulating electrodes in the medial forebrain region near the point of intersection with the lateral hypothalamic area. Each S was individually stimulated with a 60-Hz sine wave at a rate of 30 sec on, 30 sec off to test for the ability of the intracranial stimulation (ICS) to support a stimulation bound behavior (SBB). When stable SBB was established, each of 8 Ss was tested for effects of the two drugs, one a central stimulant and one a neuroleptic, on SBB in doses shown to be effective in changing overt motor activity. Each drug could disrupt an SBB. However, neither consistently changed motor activity during the ICS. Results are inconsistent with a drive reduction theory of SBB. Support for a portion of Valenstein's species typical theory of SBB was found. Both drugs were then combined simultaneously in each S. This disrupted SBB, implying that the drugs are not antagonistic to each other with respect to SBB despite extensive pharmacological literature indicating that each has the capacity to block the central actions of the other. Results are discussed with respect to the possible site of action of ICS that produces SBB, including speculation that the 5-hydroxytryptamine neurons of the medial forebrain bundle are involved. (Journal abstract modified)

173162 Stoff, David M. Yeshiva University **Multitrial passive avoidance in rats: mescaline, shock, and ITI effects. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-24801 HC$10.00 MF$4.00 327 p.

The effects of mescaline on acquisition of multitrial step down passive-avoidance in male hooded rats were investigated. Amphetamine was used as a comparison drug. Results were analyzed in terms of step down latencies in: (1) preshock step down behavior (trial one); (2) acquisition of single trial passive-avoidance (trial two), (3) acquisition of multitrial passive-avoidance (trial two to criterion trial), and (4) retention of passive-avoidance. Two significantly consistent findings occurred: (1) mescaline produced dose dependent inhibition of preshock step down behavior, while amphetamine showed a tendency towards excitation; and (2) both drugs disrupted retention of passive-avoidance, with amphetamine producing more disruption than any dose of mescaline. Overall findings indicate that there are contrasting mescaline effects on acquisition of active and passive-avoidance, suggesting the importance of response processes involved in mescaline's effects on avoidance behavior. Amphetamine's disruptive effect on passive-avoidance supports previous findings. An alternative hypothesis, which emphasizes the importance of hallucinogenic drug - stress interaction, was extended to passive-avoidance behavior. This views mescaline as an excitatory amphetamine like response agent which induces a 'hallucinatory crisis' through the inability to differentiate the signal from that which is signalled. (Journal abstract modified)

173256 Ben-Ishay, Drori; Dahl, L. K. Department of Medicine A, Hebrew University Hadassah Medical School, Jerusalem, Israel **Behavior and sensitivity to experimental hypertension: II. lack of correlation between certain behavior patterns and hypertension in two new strains of rats.** Experimental Biology and Medicine. 144(3):857-860, 1973.

A possible relationship between certain inherited behavior patterns and susceptibility to hypertension was studied in rats. Susceptibility to desoxycorticosterone (DOCA) salt hypertension is similar in the two selectively inbreed strains that exhibit disparate explorative behavior. Two other strains selected for their respective susceptibility and resistance to DOCA-salt hypertension also show explorative behavior. Inheritance of a hypertensive trait appears to be unrelated to inheritance of a specific explorative behavior in these rats. 6 references. (Author abstract modified)

173727 Gay, Patricia Eileen. Rutgers University - The State University of New Jersey **Inhibitory effects of pre- and post-test d-amphetamine on mouse-killing by rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27926 HC$10.00 MF$4.00 127 p.

Relationships between feeding, learned aversion, and amphetamine induced inhibition of predatory killing were investigated in rats. In one experiment, the effects of d-amphetamine injections in producing learned avoidance of predatory muricide were studied by pairing killing with post-killing injections, and inhibition produced in this

manner was compared to that produced by pretest injections. Experiments two and three extended these findings to pilocarpine induced killers. An attempt was made to separate mechanisms involved in pretest and posttest inhibition in experiment four, while the effects of change in feeding patterns on initiation of pilocarpine induced killing was assessed in experiment five. Experiment six demonstrated that a failure to find an overall deprivation effect facilitating the initiation of killing might be attributable to the anorexic properties of pilocarpine. Change in housing conditions did not appear to inhibit pilocarpine induced killing, as demonstrated in experiment seven. Experiment eight examined the hypothesis that the amygdala is the central target site for amphetamine inhibition of killing. Overall findings suggest that pretest d-amphetamine injections inhibit predatory killing by a direct pharmacological action on some target site or sites, while posttest injections produce a learned aversion to such killing. (Journal abstract modified)

173748 MacPhail, Robert Campbell. University of Maryland **Effects and interactions of scopolamine and d-amphetamine on schedule-controlled responding in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-28869 HC$10.00 MF$4.00 125 p.

The effects of scopolamine and d-amphetamine on rats' schedule controlled responding were investigated in Ss trained under a multiple fixed-interval 1 min (FI 1-min), fixed-interval 5 min (FI 5-min) schedule of milk reinforcement. In experiment one, the effects of scopolamine and methylscopolamine on the schedule performances were studied. Experiment two studied the effects of d-amphetamine on schedule performances. Selected doses of d-amphetamine and scopolamine were administered in combination in experiment three. Overall results indicate that the effects of the two drugs on the rats' performances were similar in many respects. They differed, however, in their effects on the temporal distribution of responses within the fixed-intervals. The effect of each drug depended on the dose as well as the parameter value of the fixed-interval schedule. No simple additive principle could characterize all the effects of the combined doses of the two drugs. (Journal abstract modified)

173749 Marshall, Keats E. University of California, San Francisco **The effects of intracaudate injections of chlorpromazine on conditioned avoidance and self stimuation behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-29932 HC$10.00 MF$4.00 85 p.

The role of the caudate - putamen complex (CNP) in the mediation of two well established effects of systemically administered chlorpromazine, the interference with performance on conditioned avoidance responding and suppression of self-stimulation behavior, was investigated in rats. In experiment one, two groups of male rats were implanted bilaterally with injection cannula directed to cortical areas overlying the CNP, or, overlying the posterior dorsal hippocampus (DHPC), and four brain areas were injected with the drug. Ss were trained in a one way active avoidance task and tested for drug effects. In experiment two, two groups of Ss were implanted as in experiment one, and, in addition, received a stimulating electrode placed in the lateral hypothalamus and trained to lever press for electrical stimulation of the hypothalamus on a continuous reinforcement schedule. Results provide further support for the thesis that CNP is a site of action for chlorpromazine, with doses of 200-to 500 micrograms resulting in catalepsy. Injections to the cortical areas overlying the CNP did not cause catalepsy or interference with avoidance performance. Injections to the DHPC, however, produced a dose related interference with avoidance performance not significantly different from that obtained in the CNP. This suggests that chlorpromazine also has other sites of action for some or all of its effects. (Journal abstract modified)

173791 Bigelow, Valerie Teresa Nigro. University of Minnesota **The effects of mescaline administered before or during embryogenesis upon the hatchability and behavior of the chick. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-25583 HC$10.00 MF$4.00 67 p.

Three experiments were conducted to determine the effect of various doses of mescaline, administered before or during development, on the domestic fowl, upon hatchability and behavior. Doses of between 1 and 100mg/kg produced a dose related decrease in hatchability of eggs when given before incubation. When day of injection of 10mg/kg doses was varied, injecting on day 3 of development produced the greatest decrease in hatchability (to 67% of saline control). Mescaline

treatment also produced several effects termed 'behavioral teratology.'These included in increase in open field activity when measured at 9 days of age, but not at 4.5days, and a superiority in detour responding from 7 to 17 days of age. None of the doses affected sex ratio or weight or produced any physical abnormalities. Results are the first to demonstrate that a hallucinogen, administered prior to or during embryonic development, can have postnatal behavioral effects. They also demonstrate that the method of Sparber and Shideman is a reliable and valid test of behavioral teratology. (Journal abstract modified)

174008 Thompson, Donald M.; Corr, Peter B. Department of Pharmacology, Georgetown University School of Medicine and Dentistry, 3900 Reservoir Road, Washington, DC 20007 **Behavioral parameters of drug action: signalled and response-independent reinforcement.** Journal of the Experimental Analysis of Behavior. 21(1):151-158, 1974.

The behavioral parameters of drug action were studied in pigeons. Four pigeons were initially trained under a multiple variable interval 1 min variable-interval 1 min schedule of food reinforcement. For two of the pigeons, a signal was then presented whenever the reinforcer was available in one component; this resulted in positive contrast. For the other two pigeons, the reinforcer was presented independently of responding on a variable time schedule in one component; this resulted in negative induction. After 30 to 50 sessions, however, a similar degree of differential responding occurred under both multiple schedules, i.e.,high rates in the variable interval component and low rates in the other component. The stable performances then served as baselines for studying drug effects. In the high rate component of both multiple schedules, small doses of d-amphetamine increased responding, whereas larger doses decreased responding. In the low rate component of both multiple schedules, there was no rate increasing effect at any dose of d-amphetamine; such an effect was found, however, with phenobarbital at a dose that decreased responding in the high-rate component. The drug effects thus depended on the interaction of pharmacologic variables (specific drug and dose) with behavioral variables (schedule components). 21 references. (Author abstract)

174034 Boggan, W. O.; Freedman, D. X.; Appel, J. B. Dept. of Psychiatry and Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **p-Chlorophenylalanine-induced alterations in the behavioral effects of 5-hydroxytryptophan.** Psychopharmacologia (Berlin). 33(4):293-298, 1973.

Pretreatment of rats with p-chlorophenylalanine methyl ester (PCPA-ME) causing a normally noneffective dose of 5-hydroxytryptophan (5-HTP) to disrupt bar pressing at times when serotonin (5-HT) concentration is low was examined. There does not appear to be any correlation between the initial, behaviorally disruptive effects of PCPA-ME and the action of this compound of 5-HT biosynthesis. 22 references. (Author abstract)

174035 Nielsen, Erik B.; Lyon, Melvin. Central Laboratory, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Drinking behaviour and brain dopamine: antagonistic effect of two neuroleptic drugs (pimozide and spiramide) upon amphetamine- or apomorphine-induced hypodipsia.** Psychopharmacologia (Berlin). 33(4):299-308, 1973.

Hypodipsia produced by injection of d-amphetamine or apomorphine in rats was antagonized by two DA specific neuroleptic drugs, Pimozide and Spiramide, respectively. Pimozide revealed a maximal amphetamine antagonistic effect at dose levels between 0.1-0.4mg/kg. Hypodipsia could also be produced by Pimozide alone in doses greater than 1.0mg/kg. Pretreatment of the apomorphine induced hypodipsia with 0.05 mg/kg Spiramide also reliably counteracted drinking deficits. There was evidence for a slight initial effect of drinking position, but the general form of the dose response curve was not greatly altered. Dopamine effects cannot easily be excluded from a role in the control of drinking. The primary role often accorded norepinephrine in relation to amphetamine effects should be reexamined with respect to the specific behavioral functions which are altered. 31 references. (Author abstract modified)

174038 Kulkarni, S. K.; Dandiya, P. C. Department of Pharmacology, S.M.S. Medical College, Jaipur-302004, India **Effects of antidepressant agents on open field behaviour in rats.** Psychopharmacologia (Berlin). 33(4):333-338, 1973.

Influence of acute and chronic administration of two types of antidepressant drugs, i.e.,tricyclic compounds and monoamine oxidase inhibitors

(MAOIs), on the Open Field behavior in rats was examined. Two types of stereotyped behavior were observed in the open field test, namely simple stereotype (ambulation) and complex stereotype (rearing). Chronic administration of MAOIs primarily caused an increase in the simple stereotyped behavior, while tricyclic compounds on repeated administration selectively increased complex stereotyped behavior. The Open Field behavior of rats due to MAOIs is comparable to hallucinogens while the pattern seen with tricyclic agent differs from MAOIs and other central nervous system stimulant drugs. 19 references. (Author abstract)

174125 Yanagita, Tomoji; Takahashi, Saburo. Department of Psychopharmacology, Central Institute for Experimental Animals, 1433 Nogawa, Kawasaki, Japan **Dependence liability of several sedative-hypnotic agents evaluated in monkeys.** Journal of Pharmacology and Experimental Therapeutics. 185(2):307-316, 1973.

Dependence liability of 10 drugs was tested in rhesus (Macacca mulatta) monkeys. Barbital withdrawal signs are suppressed by pentobarbital, alcohol, chloroform, meprobamate, diazepam, chlordiazepoxide, and oxazolam. With the exception of chloroform and meprobamate, the drugs produce physical dependence in naive monkeys and marked barbiturate like withdrawal signs. Depression and severe withdrawal signs in some monkeys are observed with pentobarbital-Ca and alcohol. By the criteria of the experimental design, benzoctamine and perlapine are found to be dependence free drugs. 13 references. (Author abstract modified)

174133 Plenge, Per K.; Mellerup, Erling T.; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark **Weight gain in lithium-treated rats.** International Pharmacopsychiatry (Basel). 8(4):234-238, 1973.

Weight gain in lithium treated rats is discussed. It is suggested that the weight gain seen in lithium treated patients can also be seen in rats during long-term lithium treatment. A study which indicates that the weight gain is in accordance with the effects of lithium on intermediary metabolism, and may be used as an indicator of proper experimental conditions is described. 13 references. (Author abstract modified)

174604 Krsiak, M. Institute of Pharmacology, Albertov 4, Prague 2, 128 00, Czechoslovakia **Behavioral changes and aggressivity evoked by drugs in mice.** Research Communications in Chemical Pathology and Pharmacology. 7(2):237-257, 1974.

The kinds of aggressive behavior a particular drug stimulates in mice are studied to achieve a better understanding of the behavioral effects of drugs. Many compounds from the listed classes of neuropsychotic drugs were found to increase aggressive behavior in aggressive mice when they were confronted with aversive stimulation. Ethyl alcohol and barbital might produce aggressive behavior in mice which usually do not respond aggressively to aversive stimulation. Drugs stimulate natural aggressive behavior in mice when the initial level of aggressiveness is not too high and they are given in low doses. There has been a satisfactory agreement between the aggression facilitating effects of drugs in mice and those of other species including man. 193 references.

174607 Spaulding, Theodore C.; Dewey, William L. Dept. of Pharmacology, School of Medicine, University of Minnesota, Minneapolis, MN **The effects of phenitrone, a reported hashish antagonist, on the overt behavior of cats.** Research Communications in Chemical Pathology and Pharmacology. 7(2):347-352, 1974.

The compound phenitrone, which has been reported to be a hashish antagonist in mice, rats and dogs, was tested for behavioral effects on cats. Cats receiving phenitrone 10-80mg/kg I.P. exhibited an alteration of their ongoing steady state pattern of behavior. At doses from 20-80mg/kg the cats showed a marked increase in vocalization and excitement and a disruption of autonomic and somatomotor functions. Phenitrone exhibited interesting behavioral effects in cats which resembled behavior induced by several known psychotropic drugs as mescaline and chlorpromozine in this species. 9 references. (Author abstract modified)

174763 Broekkamp, C. L. E.; Honig, W. M. M.; Pauli, A. I.; Van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **Pharmacological suppression of eating behavior in relation to diencephalic noradrenergic receptors.** Life Sciences (Oxford). 14(3):473-481, 1974.

The effect of the anorexigenic agents fenfluramine and dexamphetamine was studied on the eating behavior elicited by unilateral injections of noradrenaline in the perifornical area of the rat brain. Both agents were able to inhibit the eating responses. Bilateral injections of the alpha-adrenergic receptor blocker phentolamine were performed into the perifornical area and the effect on eating behavior of rats under three different deprivation conditions was studied. Depression of eating behavior by phentolamine was most pronounced in the group of undeprived rats that were given mealworms and absent in the group of rats who were deprived of food for 24 hours. These results are discussed in relation to the role of the noradrenergic system in the regulation of food intake. 19 references. (Author abstract)

174768 Patni, S. K.; Dandiya, P. C. Department of Pharmacology, S. M. S. Medical College, Jaipur 302004, India **Apomorphine induced biting and fighting behaviour in reserpinized rats and an approach to the mechanism of action.** Life Sciences (Oxford). 14(4):737, 745, 1974.

The biting and the fighting responses induced in rats by apomorphine alone, and reserpine plus apomorphine combination, respectively, are discussed. These effects could be blocked completely by a dopamine receptor blocking agent. Dopamine, norepinephrine and clonidine given intraperitoneally or intraventricularly failed to induce these responses. Chemical agents known to increase the concentration of dopamine in the brain induced the biting, but not the fighting, response. These behavioral patterns were more intense due to apomorphine in the rats pretreated with reserpine and dopamine or alpha-methyltyrosine and reserpine combinations. It is suggested that (1) the receptors on which apomorphine acts may be called 'Apomorphine Receptor' rather than 'Dopamine Receptor,' and (2) dopamine incompletely activates these receptors, which are sensitized in the absence of catecholamines and induce a higher degree of stereotyped behavior. 23 references. (Author abstract modified)

174829 Davies, J. A.; Redfern, P. H. School of Pharmacy, The University, Bath, United Kingdom **The effect of dopamine-antagonists and amantadine on the acquisition of the conditioned avoidance response in rats.** Journal of Pharmacy and Pharmacology (London). 25(Supplement):128P, 1973.

The effect of amantadine on the acquisition of a conditioned avoidance response (C.A.R.)in rats pretreated with haloperidol and pimozide, two reputedly specific dopamine receptor antagonists, was investigated. It was found that pimozide and haloperidol produced dose dependent decreases in the number of correct responses when compared to control animals receiving distilled water. Amantadine reversed the inhibitory effects of both pimozide and haloperidol. These results suggest that catecholamines, especially dopamine, are essential for the acquisition of the C.A.R. in that those drugs which specifically block the dopamine receptor inhibit the establishment of C.A.R. If amantadine is given with the dopamine antagonists, the blockade is overcome. 3 references.

174830 Davies, J. A.; Navaratnam, V.; Redfern, P. H. School of Pharmacy, The University, Bath, United Kingdom **The effect of phase-shift on the passive avoidance response in rats, and the modifying effect of chlordiazepoxide.** Journal of Pharmacy and Pharmacology (London). 25(Supplement):129P, 1973.

The effects of phase shift on the passive avoidance response (PAR) in rats and the modifying effect of chlordiazepoxide was investigated. The effect of librium on phase shift was studied by replacing the normal drinking water with solutions for the 5 days after phase shift. These concentrations given to nonphase shift animals did not significantly affect the PAR. Phase shifted animals receiving librium showed a dose dependent increase in the acquisition of the PAR when tested at 1200 h on day 5. These animals appeared to have adapted to the new light - dark cycle. Librium therefore appeared to produce a more rapid resynchronisation of the 24 h rhythm in PAR and to prevent the period of asynchrony which normally precedes the new steady state, and which is characteristically associated with behavioral disturbances. 6 references.

174860 Mabry, Paul D.; Campbell, Byron A. Department of Psychology, Princeton University, Princeton, NJ 08540 **Ontogeny of serotonergic inhibition of behavioral arousal in the rat.** Journal of Comparative and Physiological Psychology. 86(2):193-201, 1974.

The age at which serotonergic inhibition of behavioral arousal first appears in rats, was studied. Results are interpreted as evidence for the delayed maturation of a serotonergic inhibitory system that modulates behavioral arousal.

Neonatal rats, ranging from 10 to 25 days of age, were injected with para-chlorophenylalanine, which depletes brain serotonin, and then tested for locomotor effects after periods of zero, 24, 48, and 72 hours. Depletion of serotonin increased behavioral arousal in 15-, 20-, and 25-day-old animals, but not in those that were 10 days old. Para-chlorophenylalanine potentiated the locomotor activity induced by amphetamine, but again 10-day-old animals did not show the effect. 53 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

167361 Carlson, Gary P. Dept. of Pharmacology and Toxicology, College of Pharmacy, Univ. of Rhode Island, Kingston, RI 02881 **Effect of phenobarbital and 3-methylcholanthrene pretreatment on the hepatotoxicity of 1,1,1-trichloroethane and 1,1,2-trichloroethane.** Life Sciences (Oxford). 13(1):67-73, 1973.

The effect of phenobarbital and 3-methylcholanthrene (3-MC) pretreatment on the hepatotoxicity of 1,1,1-trichloroethane and 1,1,2-trichloroethane was studied in rats. The toxicity of the 1,1,2- isomer was increased to a greater extent than that of the 1,1,1- isomer. 3-MC pretreatment did not result in increased hepatotoxicity. 14 references. (Author abstract modified)

168498 Tanase, Hisao; Hirose, Kouichi; Suzuki, Yoshio. Research Laboratories, Sankyo Co., Ltd., Japan **The safety test of 10-chloro-11b-(2-chlorophenyl)-2,3,5,6,7,11b-hexahydrobenzo (6,7)-1,4-diazepino(5,4-b)oxazol-6-one (CS-370): second report, effect of C-370 upon the development of pre- and post-natal offsprings of experimental animals.** Annual Report of Sankyo Laboratories (Tokyo). 23:180-191, 1971.

The effect of CS-370 on the prenatal and postnatal development of mouse and rat offspring were studied, based on an experiment in which pregnant mice and rats were orally treated with CS-370 (3 to 600/mg/kg/day) for 6 days between the 7 and 12th day of pregnancy in mice and the 9 and 14th day in rats. The fetuses were removed from the dams on day 18 of pregnancy in mice and day 20 in rats, and some offspring were allowed to be delivered and to survive until sexual maturity. CS-370 neither revealed any lethal or teratogenic effects on these embryos nor affected the development and behavior of the surviving offspring. 9 references. (Author abstract modified)

168862 Roizen, M. F.; Moss, Jonathan; Henry, D. P.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Effect of general anesthetics on systemic catecholamine concentration I: halothane. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 16 p.

The effect of halothane on levels of plasma catecholamines was studied in the Sprague-Dawley rat using a new sensitive radioactive isotopic derivative assay for catecholamines. The levels of catecholamines in the plasma obtained from blood withdrawn from arterial cannulae of wakeful animals was similar to the values found in these animals 3 weeks later, when blood was obtained after decapitation. Both these values were much higher than those found in anesthetized animals. Under halothane anesthesia, the plasma levels of catecholamines paralleled blood pressure changes. The study suggests that many of the cardiovascular effects seen with halothane may be due to its effect on systemic sympathetic neuronal discharge and that the arrythmias seen upon lightening of halothane anesthesia may be the result of a rapidly developing form of denervation supersensitivity. 13 references. (Author abstract modified)

169688 Koppanyi, Theodore; Maling, Harriet M. Department of Pharmacology, Georgetown University School of Medicine, Washington, DC 20007 **Temperature-dependent toxicity of adrenergic agonists in mice as a basis for treating d-amphetamine poisoning.** Proceedings of the Society for Experimental Biology and Medicine. 144(2):575-580, 1973.

The effects of two amines and three catecholamines in treating acute d-amphetamine poisoning is studied. These adrenergic agonists were studied at room and 4 degrees temperature in an attempt to find a rational treatment for clinical d-amphetamine poisoning, expecially in children. Body temperature, salivation, and death rate of rats in response to the adrenergic agonists were measured. Comparisons of LD50 values at room temperature and 4 degrees were made by probit analysis. It was found that the catecholamines were more toxic at the higher temperature, whereas some injected mice were protected by exposure to cold. Mice injected with d-amphetamine at room temperature salivated profusely and convulsed, but the surviving animals were protected from death by transfer after a half an hour to 4 degrees. This study is seen to conform with others concerning the effect

of drugs depending on ambient temperatures. 24 references. (Author abstract modified)

170464 Cottrell, John C.; Sohn, Seung S.; Vogel, Wolfgang H. Thomas Jefferson University, 1020 Locust St., Philadelphia, PA 19107 **Toxic effects of marihuana tar on mouse skin.** Archives of Environmental Health. 26(5):277-278, 1973.

The effects of marihuana smoke condensate on the histological properties of mouse skin were studied in order to discover whether such condensate might be carcinogenic. Tar obtained from cannabis sativa was dissolved in acetone and painted on albino Swiss mice and black and white f-1 hybrid mice; 30 mice of each strain were used. Microscopic examination of the skin showed squamous metaplasia of the sebaceous glands and hyperkeratosis, acanthosis, and in some cases, enlargement and hyperchromasia of nuclei and poor cellular polarity in the squamous epithelium. It is concluded that since metaplasia of sebaceous glands correlates with carcinogenicity, cannabis sativa tar might prove to be carcinogenic. 4 references. (Author abstract modified)

171792 Martin, Dean F.; Heyl, Michael G.; Doig, Marion T., III. Department of Chemistry, University of South Florida, Tampa, FL 33620 **Effect of selected beta-diketones on lithium fluxes of bovine red blood cells.** Life Sciences. 12(6):241-151, 1973.

The effect of beta-diketones on lithium fluxes of bovine red blood cells was studied. Apparent cell concentration increased rapidly with time until a maximum was attained, then decreased to a constant or equilibrium value. The correlation between apparent maximum cell uptake and effective external lithium concentration (external lithium concentration divided by hematocrit) was significant. The equilibrium cell concentration showed a correlation with lithium gradient (ratio of internal and external lithium concentrations). The effect of dipivaloylmethane (DPM) on lithium influx and efflux was studied. The chelating agent enhanced the rate of lithium removal from lithium loaded cells. 14 references. (Author abstract modified)

172598 Nadeau, Reginald; de Champlain, Jacques. Centre de Recherche en Sciences Neurologiques, Dept. de Physiologie, Faculte de Medecine, Universite de Montreal, Montreal Quebec, Canada **Comparative effects of 6-hydroxydopamine and of reserpine on ouabain toxicity in the rat.** Life Sciences (Oxford). 13(12):1753-1761, 1973.

The toxic effects of ouabain were compared in normal, and in reserpine pretreated rats. Reserpine significantly reduced the lethality of 6-hydroxy-dopamine (6-OH-DA) and reserpine pretreated rats. Reserpine not. Since reserpine, but not 6-OH-DA, does cross the blood brain barrier it is suggested that the protective effects of reserpine might be related to its action on the central nervous system. 13 references. (Author abstract modified)

173548 Yokotani, Hajime; Amori, Toshio; Tanda, Masaru; Ishii, Harumitsu; Nagawa, Yuji. Takeda Research Laboratories, Osaka, Japan **Acute toxicity of 8-chloro-6-phenyl-4H-s-triazolo 4,3-a 1,4 - benzodiazepine (D-40TA) in mice, rats, rabbits and dogs.** Journal of the Takeda Research Laboratories (Osaka). 32(2):152-157, 1973.

Toxicity of D-40TA was investigated in mice, rats, rabbits and dogs. Bodyweights of the animals are detailed along with dosages administered. Two out of four male dogs died after oral administration of 1000mg/kg of D-40TA. However, frequent occurrence of vomiting in dogs prevented the precise determination of the LD -50 value. Symptoms observed in each mode of administration are described. 2 references. (Author abstract modified)

174608 Karler, Ralph; Cely, William; Turkanis, Stuart A. University of Utah College of Medicine, Salt Lake City, UT 84132 **A study of the relative anticonvulsant and toxic activities of delta9-tetrahydrocannabinol and its congeners.** Research Communications in Chemical Pathology and Pharmacology. 7(2):353-358, 1974.

The relative anticonvulsant activity and motor toxicity of some cannabinoids is compared to determine whether the anticonvulsant and toxic properties are separable. Specifically, delta9-tetrahydrocannabinol is compared to cannabidiol and dimethylheptylpyran. Anticonvulsant activity was determined in a maximal electroshock text and toxicity in a bar-walk test. Results indicate that the anticonvulsant and toxic properties of these cannabinoids are separable. The order of relative toxicity from greatest to least was dimethylkeptylpyran, delta9-tetrahydrocannabinol, and cannabidiol. 14 references. (Author abstract modified)

174855 Yamashita, Junko; Makino, Katashi, Dept. of Biochemistry, Jikei University School of Medicine, Japan **Behavioral and electroencephalo-**

graphic studies on thiosemicarbazide-induced seizure in rabbits. Jikeikai Medical Journal (Tokyo). 18(3/4):99-107, 1971.

Thiosemicarbazide (TSC) induced seizure was studied by electroencephalography (EEG) and correlated behavioral observations in rabbits with chronic indwelling brain electrodes. Following behavioral restlessness, generalized seizure discharge usually appeared initially in the neocortical systems and subsequently extended to other brain areas. Localized seizure discharge was usually limited to the neocortical areas and was not accompanied by signs of behavioral seizure. Behavioral seizure was sometimes preceded by EEG seizure. Running fits, which followed EEG activation, were distinguished from EEG seizure discharges. In TSC treated animals, EEG patterns before the first seizure discharge were not substantially different from those of the control, but the sleep wakefulness cycles tended to the arousal condition. 4 references. (Author abstract modified)

174961 Phillips, Richard Norman. Indiana University, Bloomington, IN **Toxicology of delta-9-tetrahydrocannabinol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-2746 HC$10.00 MF$4.00 167 p.

The acute toxicity of delta9-tetrahydrocannabinol (THC) was evaluated in rats and mice by determining oral, intravenous, and intraperitoneal LD 50 values. After 15 days of daily THC administration, during a 30 day study, rats receiving 30mg/kg each day showed decreases in weight gain and increases in sensitivity to the effects observed following the administration of THC. Central nervous system depressant properties of THC were indicated by prolongation of ethanol or hexobarbital induced sleep in rats and mice. Central nervous system stimulatory actions were also exhibited by THC since it prolonged the stimulation of motor activity in mice induced by methamphetamine or caffeine. THC administered acutely was not effective in abolishing or shortening the length of convulsions from electroshock, pentylenetetrazol, or strychnine in mice. However, after prolonged treatment of mice with THC, acute administration was effective in reducing the toxic effects of pentylenetetrazol. Acute treatment of mice with THC did impair their ability to remain on a continually rotating rod for 90 seconds. (Journal abstract modified)

06 METHODS DEVELOPMENT

169932 de Alburquerque, Iracema Campos; de Alburquerque, Manuel Antonio. Facultad Catolica de Medicina de Porto Alegre, Brazil **/Psychopharmacological research: some methodological problems./** Investigacion psicofarmacologica. Algunos problemas metodologicos. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 18(3):186-188, 1972.

The lack of methodology in scientific psychopharmacological research is discussed. Terminology for describing research is inadequate, imprecise, unrelated, and nonstandardized. Present semeiology is inadequate for purposes of identifying and quantifying psychopathologic changes. The substitution of symptoms creates a technical problem for the establishment of stable criteria for improvement. Variables are a consequence of these shortcomings, and of the complexity of the material under study. Testimony of patients is described as untrustworthy because of impressions, affective distortion, and lack of independent criteria for suffering and detrimental effects. Collateral and toxic effects are difficult to define. Lack of specific indications for each drug is a cause of deceptive results. The need for methodological tools to ascertain the purely pharmacological action of any drug is cited as mandatory for absolute conclusions.

170112 Eckman, Walter W.; Patlak, Clifford S.; Fenstermacher, Joseph D. Theoretical Statistics and Mathematics Section, NIMH, Bethesda, MD 20014 **A critical evaluation of the principles governing the advantages of intraarterial infusions.** Bethesda, MD, NIMH, 1973. 45 p.

The principles governing the advantages of intraarterial infusions were analyzed in an attempt to provide adequate evidence supporting the clinical use of such infusions as a method of drug administration. The advantages gained in increased total drug delivery and increased drug effectiveness in the region supplied by the infused artery, as well as reduced systemic drug delivery following intraarterial infusion, are stressed. Simplifying assumptions allowed precise determination of the advantages of regional or systemic drug delivery when drug delivery is evaluated by the total time integral of drug concentration, and simplified experimental approaches are suggested for precise measurement of these advantages. Drug effectiveness is more difficult to evaluate because of the usual nonlinear relationship between effect and

concentration. However, certain relationships between the advantage of regional drug delivery and of regional drug effects are elucidated. The analysis offers new insight into the factors which determine the value of intraarterial drug administration. 13 references. (Author abstract modified)

170302 Usdin, Earl. Pharmacology Section, Psychopharmacology Research Branch, Div. of Extramural Research Programs, NIMH, Rockville, MD **Research on super-sensitive laboratory methods in Sweden.** In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 156-160).

A method for detecting very small amounts of drugs or other chemicals in the body is reported. Mass fragmentography is a technique in which the mass spectrometer is used as a chromatographic detector; advantage is taken of the physiochemical characteristics of the compounds in order to achieve separation, specificity and sensitivity. The work described includes: the development of new supersensitive analytical methodologies; the application of such methodologies to the analysis of natural products; and the application of such methodologies to metabolic studies. Studies of alkaloids, hallucinogens, biochemical intermediates, therapeutic drugs, antidepressants and some unknowns are described. 1 reference.

170839 Sethi, Manohar L.; Rao, G. Subba; Kapadia, Govind J. Department of Biomedicinal Chemistry, College of Pharmacy and Pharmacal Sciences, Howard University, Washington, DC 20001 **Peyote and related alkaloids XVI: synthesis of 3,4,5-trimethoxyphenylalanine, an amino analog of mescaline.** Journal of Pharmaceutical Sciences. 62(11):1802-1806, 1973.

Contrary to an earlier literature report, acid hydrolysis of diethyl gamma-acetamido-gamma-3,4,5-trimethoxybenzylmalonate during the synthesis of 3,4,5-trimethoxyphenylalanine has been shown to lead to a mixture of products. The major hydrolysis products were isolated and identified by NMR and mass spectrometry as 3,4,5-trimethoxyphenylalanine (34%), 4-hydroxy-3,5-dimethoxyphenylalanine (13%), 3-hydroxy-4,5-dimethoxyphenylalanine (8%), and 3,4-dihydroxy-5-methoxyphenylalanine (5%). Under basic conditions, the acetamidomalonate ester as well as its formamido analog, obtained by the condensation of trimethoxybenzyl chloride and diethyl formamidomalonate, gave low yields (5-7%) of the required trimethoxyphenylalanine. However, no phenolic side products were formed under basic conditions. An efficient alternative synthesis of 3,4,5-trimethoxyphenylalanine has been accomplished; it involves the condensation of hydantoin with trimethoxybenzaldehyde followed by hydrogenation and basic hydrolysis of the resulting 5-(3,4,5-trimethoxybenzylidine) hydantoin. GC-mass spectrometric examination of the peyote amino acid fraction gave no evidence for the presence of trimethoxyphenylalanine and other trioxygenated phenylalanine analogs obtained during these synthetic studies. 7 references. (Journal abstract)

170840 Loeffler, Larry J.; Pierce, Jack V. Division of Medical Chemistry, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27514 **Radioimmunoassay for lysergide (LSD) in illicit drugs and biological fluids.** Journal of Pharmaceutical Sciences. 62(11):1817-1820, 1973.

A simple and convenient radioimmunoassay system was developed for the qualitative detection and quantitative determination of lysergide (LSD) in illicit drugs, human plasma, serum, or urine. The method utilizes a commercially available tritiated lysergide and specific antiserum, which can be obtained in large quantities from sheep after immunization with a lysergic acid human serum albumin conjugate. Quantities of lysergide as low as 1ng/ml can be determined in plasma, serum, or urine, and lower levels can be detected qualitatively. The sensitivity of the assay is limited by the specific activity of the commercially available tritiated compound. Antibody cross-reactivity and, thus, interference in the assay were observed with other highly similar ergot alkaloids, such as ergonovine, methylergonovine, and ergotamine, but not with simpler indole structures. 4 references. (Journal abstract)

171260 Roe, Tae Sun. School of Medicine, Kyung Hee University, Seoul, Korea **Study on the psychopharmacological assay of centrally acting drugs in rats.** Korean Central Journal of Medicine (Seoul). 22(3):333-335, 1972.

Chlorpromazine and other drugs having tranquilizing action on the central nervous system of rats were studied to determine whether avoidance conditioning utilizing the shuttlebox is an effective method of standardizing tranquilizing action. The benzodiazepine group was chosen as one of the centrally acting drugs and its effect on the acquisition and extinction of avoidance conditioning in rats compared with that of chlor-

promazine was examined. It was observed that the tranquilizing action of chlorpromazine is more effective in the rat than that of the benzodiazepine group. However, due to the poor results obtained, it is felt that the instrumental avoidance conditioning procedure used is not a suitable method for the standardization of the tranquilizing action of the drugs of the benzodiazepine group as centrally acting medicines. 9 references. (Journal abstract modified)

173536 Shostak, M. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Psychoactive drugs: immunoassay and localization.** Final Report, NIMH Grant MH-21297, 1973. 4 p.

Immunoassay and localization of psychoactive drugs are discussed. Methods of coupling phenothiazines to carrier proteins have been developed and the resultant hapten - protein conjugates shown to be potent antigens in animals. High titers of hapten specific antibodies to phenothiazine - protein conjugates were elicited in both rabbits and guinea pigs with standard immunization procedures. Results demonstrate that phenothiazines can be used as haptens to elicit antisera which are suitable for radioimunoassay of chlorpromazine at 25 nanogram level.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

167334 Wilson, Roy D.; Allen, Charles R.; Creson, Daniel; Schmitt, Richard; Barratt, E.; Traber, D. L. Department of Anesthesiology, University of Texas Medical Branch, Galveston, TX 77550 **Operant behavior and neurophysiological observations of normal human volunteers receiving CL-1848C, a new dissociative anesthetic.** Texas Reports on Biology and Medicine. 31(2):239-248, 1973.

A study of 13 normal human volunteers which confirms the safety of CL-1848C (Etoxadrol), a new dissociative anesthetic, is described including operant behavior and neurophysiological observations. It is concluded that in cognitive or motor function tests, there was no change in rank order performance of the individuals in the postdrug period as compared to their predrug period. Psychological testing failed to reveal any evidence of personality derangement or toxicity from the drug. Likewise, psychological evaluation revealed no trauma to the psyche from the drug or the design of the experiment. Electroencephalographic interpretation revealed an interesting and unusual feature of the drug: all records remained essentially normal but changed from the awake pattern to a drowsy or light sleep record without other evidence of drug imposition. Unusual dreams or experiences were reported, but did not affect subject acceptance of the drug. 18 references. (Journal abstract modified)

168499 Takagi, Hiromu; Kamioka, Toshiharu; Kobayashi, Shinsaku; Kumakura, Seiji; Ohshima, Takeshi; Nakayama, Koichi; Iizuka, Yoshio; Inazu, Yoshihiko. Research Laboratories, Sankyo Co., Ltd., Japan **Pharmacological studies of oxazolazepam, a new psychotropic agent (second report): general pharmacology and subacute toxicity.** Annual Report of Sankyo Laboratories (Tokyo). 22:286, 1970.

The pharmacological activities and subacute toxicity of oxazolazepam and chlordiazepoxide are compared. Oxazolazepam causes slight hypotension and depression of heartrate in larger doses but has no significant effect on respiration, ECG and responses to autonomic drugs. These effects are weaker than those of chlordiazepoxide. Oxazolazepam also exhibits more effects on isolated organs than does chlordiazepoxide. Other effects, such as miosis, hypothermia, constipation and physical dependence liability are induced to a lesser degree by oxazolazepam. Emetic, antiinflammatory and diuretic actions are not caused by either. Subacute toxicity induced by 5 week administration of oxazolazepam is definitely less than that induced by chlordiazepoxide. (Author abstract modified)

169297 Santos, Mario R.; Romi, Juan C. San Juan 3125, Buenos Aires, Argentina **Lorazepam: clinical trial with a new benzodiazepine.** Psychosomatics. 14(5):298-301, 1973.

The results of clinical tests on a new benzodiazepine, lorazepam, on 26 ambulatory and hospitalized patients in whom anxiety was an important factor in their symptomatology are presented. The chemical structure of lorazepam is given. The major advantages of lorazepam are: (1) marked anxiolytic effect at very low dosages (4mg/day); (2) its anxiolytic effect is rapid and can be observed in the first week of treatment; and (3) it practically lacks serious side-effects at usual dosages. 17 references.

172735 Bjerke, K.; Faurbye, A.; Kirk, L. no address **/One year of clinical experience with large doses of 10 percent flupenthixol decanoate (Lu 1705)./** Et ars klinisk erfaring med Flupenthixoldecanoat 10 percent (Lu 1705) i hoj dosering. Nordisk Psykiatrisk Tidsskrift (Odense, Denmark). 26(6):363, 1972.

Results of clinical tests of flupenthixol decanoate 10% (Lu 1705) in doses of 100mg, or more, on 99 psychotic female patients are reported. Manic patients received four injections of 250mg Lu 1705 for 8 days, the rest 130mg once a week for 18 weeks. Treatment was found to be better than previous treatments in over half the patients. Good results were obtained in 10 of 11 manic patients, as well as in four of 14 patients suffering from schizophreina for from 1 to 4 years. Seven of 32 patients with schizophrenia for over 5 years responded to treatment. One third of the patients showed no neurological side-effects. Lu 1706 in 100 mg doses was found to have broader neuroleptic effects than small doses. Patients were emotionally more animated as compared to behavior after earlier treatment with other neuroleptics. Further controlled research is indicated.

08 DRUG TRIALS IN SCHIZOPHRENIA

167341 Kramer, Milton; Blackwell, Barry; Roth, Thomas; Wray, Marianne. Dept. of Psychiatry, College of Medicine, Univ. of Cincinnati, Cincinnati, OH **Metiapine in acute schizophrenic patients.** Current Therapeutic Research. 15(7):465-469, 1973.

The efficacy and safety of metiapine (MP), a dibenzothiazapine derivative, in the treatment of 10 acute schizophrenics was studied. The drug was effective in alleviating psychotic symptoms within 2 weeks. Sedation was the most prominent side-effect of the drug. MP produced other unwanted effects but these effects do not appear to be very different from those found with other phenathiazines either in type or intensity. No evidence of cardiovascular, hepatic or renal impairment was observed. 6 references. (Journal abstract modified)

167342 Flemenbaum, Abraham. Dept. of Psychiatry, Univ. of Minnesota, Minneapolis, MN **Metiapine: the evaluation of the antipsychotic properties of a new neuroleptic. A pilot study.** Current Therapeutic Research. 15(7):470-472, 1973.

Antipsychotic properties of a new dibenzothiazepine neuroleptic, metiapine, were evaluated in 20 acute schizophrenic patients. Frequent problems included marked drowsiness, tachycardia with hypotension, and the necessity of increasing the medication relatively fast with accompanying extrapyramidal symptoms, all in contrast to published reports. Twelve patients showed some improvement and posttreatment ratings showed improvement at the .01 level of statistical significance. 6 references. (Journal abstract modified)

167343 Chouinard, G.; Pinard, G.; Serrano, M.; Tetreault, L. Hopital St.-Jean-de-Dieu, Montreal Gamelin, Quebec, Canada **Potentiation of haloperidol by alpha-methyldopa in the treatment of schizophrenic patients.** Current Therapeutic Research. 15(7):473-483, 1973.

Potentiation of haloperidol (HP) by alpha-methyldopa (MD) in the treatment of schizophrenic patients is discussed. An uncontrolled clinical study took place over a 4 week period. The ratio of MD to HP was 50:1. In three symptom rating scales, there was a significant improvement after 14 days of treatment which persisted until the end of the study. The hypotensive effect of the drug combination was significant only in the supine diastolic blood pressure. The sedative effect was marked in agitated patients. Some mild side-effects were noted. 7 references. (Journal abstract modified)

167676 Postel, M.; Czermack, M.; Postel, J. Hopital psychiatrique de Maison-Blanche, 7e section, 3, avenue Jean-Jaures, 93-Neuilly-sur-Marne, France **/Depressive forms of schizophrenia and experimental treatment by clomipramine./** Les formes depressives de la schizophrenie: essai de traitement par la clomipramine. Encephale (Paris). 60(4):312-334, 1971.

A 3 year study of 25 patients given clomipramine (anafranil) on an experimental basis to determine the effects of antidepressants in schizophrenia is analyzed. Case histories are detailed in an effort to establish effects definitely attributable to the drug, and those resulting from psychotherapy and chemotherapy. The few cases involved are insufficent for development of significant statistics. There were seven failures, 10 average, and eight definitely improved cases recorded. Sufficient evidence was found to encourage use of clomipramine in depressive forms of schizophrenia, but antidepressant treatment for aggressive and delirious schizophrenia must be undertaken in the hospital environment and under neuroleptic cover. Clomipramine is recommended at this time only for depressive forms, and as a neuroleptic complement and corrector. 14 references.

167817 Emmerich, David S.; Levine, Fredric M. Department of Psychology, State University of New York, Stony Brook, NY 11790 **Phenothiazine dosage levels and auditory signal detection in schizophrenia.** Science. 179(4071):405-406, 1973.

Phenothiazine dosage levels and auditory signal detection in schizophrenia are discussed in relation to results published in an earlier report by Rappaport. In the earlier study, it is felt that there is no evidence that phenothiazines have a statistically significant effect on signal detection performance within either paranoid or nonparanoid schizophrenic groups. Calculations based on the study's data suggest that there were no statistically significant effects within either group related to phenothiazine dosage. It is not possible to tell whether any given significant difference in performance was due to a difference in sensitivity or to a difference in the ability to focus attention, or both. The fact that in the difficult signal detection

condition, nonmedicated nonparanoid schizophrenics were slightly hyposensitive does not seem to provide strong support for the interpretation that they are hypersensitive under such conditions. 3 references.

167954 Presley, J. M.; Ellen, Paul; Foshee, D. P. VA Hospital, Tuskegee, AL **Sleep phenomena in schizophrenia.** Newsletter for Research in Mental Health and Behavioral Sciences. 15(4):15-17, 1973.

Differences in sleep patterns in schizophrenic patients resulting from various psychotrophic medications were studied. Mellaril, Stelazine, Thorazine, Librium, and Aventyl were used in various combinations on the patients. The results are presented in a table that compares latency to sleep, latency to first REM, % of REM, % of stage four activity, and percent of time awake. It is concluded that a meaningful description of the sleep patterns of clinically defined entities requires analysis in terms of the medication regime on which the patients are being maintained before comparing with normals. 3 references.

168313 Ananth, J. V.; Ban, T. A.; Lehmann, H. E. Douglas Hospital and McGill University, Montreal, Quebec, Canada **Potentiation of therapeutic effects of nicotinic acid by pyridoxine in chronic schizophrenics.** Canadian Psychiatric Association Journal (Ottawa). 18(5):377-383, 1973.

The administration of pyridoxine to enhance the therapeutic effect of nicotinic acid in schizophrenic patients by opening up the kynurenine cycle of tryptophan metabolism and thereby decreasing the formation of indoles was tested. The therapeutic effect of a combination of nicotinic acid and pyridoxine was compared with that of treatment with either nicotinic acid or pyridoxine alone. Of the three indices of therapeutic effects, global improvement in psychopathology scores was seen in all three groups; the number of days of hospitalization during the period of the clinical study was lower in both the nicotinic acid and the combined treatment group; and only in the combined treatment group was the daily average dosage of phenothiazine medication decreased. Thus, improvement in all three indices was noted in the combined treatment groups. Several side-effects were observed, however, indicating that the vitamins used are not completely safe. 32 references.

168320 Singh, A. N. Psychopharmacology Unit, Hamilton Psychiatric Hospital, Department of Psychiatry, McMaster University, Hamilton, Ontario, Canada **Clinical evaluation of fluspirilene as a maintenance therapy in chronic schizophrenic patients.** Canadian Psychiatric Association Journal (Ottawa). 18(5):415-419, 1973.

Fluspirilene, a new, long-acting injectable neuroleptic belonging to the diphenylbutylpiperidine series, was evaluated for efficacy in controlling symptoms of schizophrenic patients who had been stabilized with conventional neuroleptic therapy. The effects of fluspirilene in resocialization were studied, determining degree of adjustment to life outside the hospital at or near the prepsychotic level, or, in the case of a long-term resident who cannot be released, the broadening of interests and activities so that the patients function at a higher level in the hospital setting. The transition from previous drugs to fluspirilene was achieved gradually, safely, and successfully. Over 66% of the patients showed a better response to fluspirilene than to their previous neuroleptic medications. Fluspirilene proved to be an effective, long-acting injectable drug for the maintenance therapy of chronic schizophrenics. 7 references.

168836 Sakalis, G.; Chan, T. L.; Gershon, S.; Park, S. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, N. Y. Univ. Medical Center, 550 First Ave., New York, NY 10016 **The possible role of metabolites in therapeutic response to chlorpromazine treatment.** Psychopharmacologia (Berlin). 32(3):279-284, 1973.

The possible role of metabolites in the therapeutic response of chlorpromazine (CP) treatment was investigated in eight male adult schizophrenics. Clinical assessments were made weekly by a psychiatrist who was unaware of the biochemical findings. Blood samples were drawn 3 h after the first daily dose and the plasma concentrations of CP and 11 of its metabolites were assessed. Ss that responded well to treatment had high plasma levels of CP and 7-hydroxychlorpromazine and nonresponders had a high plasma levels of CP sulfoxide. Findings support the hypothesis that CP metabolites play an important role in determining clinical response to treatment. 7 references. (Author abstract modified)

169438 Stevens, Barbara C. Medical Research Council Social Psychiatry Unit, Institute of Psychiatry, De Crespigny Park, London SE5, En-

gland **Role of fluphenazine decanoate in lessening the burden of chronic schizophrenics on the community.** Psychological Medicine (London). 3(2):141-158, 1973.

The social results of a double-blind placebo controlled trial of fluphenazine decanoate administered to schizophrenic patients is presented. Among patients on placebo there was a deterioration in family relationships, which was due to an increase in aggression, noisiness, talking about delusions, and socially embarrassing behavior after withdrawal of active drug. 58 references. (Author abstract)

170637 Yagi, Gohei. Minakawa Hospital, Japan **Therapeutic approach to the approximate answers of a schizophrenic patient.** Clinical Psychiatry (Tokyo). 14(10):911-917, 1972.

Therapeutic approach to a schizophrenic patient through verbal correction and psychopharmacology is discussed. The schizophrenic patient was asked to walk back and forth on the hospital floor 30 times a session and was asked how many trips he had made. Therapy was continued for 2.5years for a total of 150 sessions. During the first year, two nurses supervised the therapeutic session alternately and the occurrence of erroneous responses differed between the two nurses. After 41 sessions, however, erroneous responses completely disappeared. During the second year, one nurse supervised the therapy under different conditions. When the nurse corrected the patient's erroneous response verbally without psychotropic drug administration erroneous responses significantly decreased. When the patient was given drugs and not verbally corrected, erroneous responses did not decrease. When psychotropic drugs and verbal correction were given, erroneous responses decreased more significantly than in instances when the patient was given verbal correction but not psychotropic drugs. 8 references.

171245 Yamauchi, Ikuro. Yamauchi Hospital, Japan **Effects of L-Dopa on schizophrenia.** Clinical Psychiatry (Tokyo). 14(10):941-949, 1972.

The effect of L-Dopa on schizophrenia was studied. Thirty schizophrenic patients, 19 to 51 years old, were treated orally with L-Dopa (300-400mg/day for 2 months) in addition to major tranquilizers which had been previously administered. L-Dopa was significantly effective in six patients, effective in eight, moderately effective in five, and noneffective in the others. The drug was especially effective in improving autistic tendency and dullness of emotion and also effective in eliminating hallucination, delusion and behavior abnormality. Patients with catatonic and hebephrenic types of schizophrenia showed more improvement than those with delusion type; no side-effects were observed. 11 references.

171505 Hollister, Leo E.; Overall, John E.; Kimbell, Isham, Jr.; Pokorny, Alex. VA Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Specific indications for different classes of phenothiazines.** Archives of General Psychiatry. 30(1):94-99, 1974.

The differential effectiveness of various phenothiazine derivatives on certain types of schizophrenic patients was examined in 320 newly admitted schizophrenic men randomly assigned to either an aliphatic, piperidine, or piperazine phenothiazine. Physicians chose drugs within the class assigned and used them to maximal clinical advantage. None of the drug classes was superior to another in total efficacy. Finer differences were that piperazines were more effective in patients who were older and who were categorized as having 'core' or 'nonparanoid' types of schizophrenia, chiefly thought disorders. The prevailing belief that these drugs are more specific antipsychotic agents was given some support. Past difficulties in replicating specific indications for antipsychotic drugs, as well as the few differences found in this study, force the clinician still to choose drugs empirically. Differing reactions of individual patients to various drugs are more likely due to differences in drug kinetics. 14 references. (Author abstract)

171507 Simopoulos, Aris M.; Pinto, Alcides; Uhlenhuth, Eberhard H.; McGee, John J.; DeRosa, Ernest R. Medical Research Dept., Crownsville Hospital Center, Crownsville, MD 21032 **Diphenylhydantoin effectiveness in the treatment of chronic schizophrenics: a double-blind controlled study with a placebo.** Archives of General Psychiatry. 30(1):106-111, 1974.

The relative effectiveness of diphenylhydantoin or placebo in treating chronic schizophrenia was examined in 76 Black male and female patients. During an 8 week treatment course, the dose of diphenylhydantoin was gradually increased from 325 to 625mg/day, for most patients. Assessment was via the Brief Psychiatric Rating Scale (BPRS), the Nurses Observation Scale for Inpatient Evaluation, and the Crownsville Psychiatric Scale (parts one and two). Statistical analyses

were done at 4 and 8 weeks. Patients on both diphenylhydantoin and the placebo deteriorated on most measures. Differences in favor of diphenylhydantoin were found for the BPRS variables, Hostility, and Thought Content. Optimal dosage of diphenylhydantoin appeared to be under 500mg, daily, since retardation and blunted affect were more predominant with diphenylhydantoin at the highest dose levels. Indications were that men with high initial disorder scores, especially for hostility, responded best. 11 references. (Author abstract)

171985 Jha, B. K.; Bhaskaran, K. Hospital for Mental Diseases, Kanke, Ranchi-6, Bihar, India **Experiences with fluphenazine enanthate in long stay hospitalised schizophrenics.** In: Some aspects of schizophrenic illness in India. Eastern Zone of Indian Psychiatric Society, 1971. 149 p. (p. 95-118).

The effect of fluphenazine enanthate injection on long stay schizophrenic patients was studied. A clinical trial was carried out in 112 schizophrenic patients with a minimum duration of illness of 2 years, a maximum of 26 years, and a mean of 10.4years. Significant improvement occurred in 32.2% of the cases, and 22.3% were made manageable in the hospital. The most encouraging results were seen in cases of paranoid schizophrenia. Side-effects were noted in 73.2% of the cases and are discussed. It is concluded that the drug is useful for some chronic schizophrenics resistant to other forms of treatment and possibly for those who show frequent relapses; it is not risky to treat the patients with the drug at home. 41 references.

172435 Imlah, Norman W. All Saint's Hospital, Birmingham, England **Schizophrenia management-the dawn of a new era.** Current Medical Practice (Bombay). 15(6):780-783, 1971.

Regularly administered doses of phenothiazine derived drugs or butyrophenones produce a satisfactory remission of the symptoms of schizophrenia, but the failure of discharged patients to take the tablets causes many to be readmitted to hospitals or clinics. Use of long-acting injectable fluphenazine decanoate is suggested as a means of treating patients on an outpatient status with permanent followup and maintenance injections at clinics. Effective management of schizophrenia in discharged patients is discussed.

172444 Shah, L. P.; Sule, S. M.; Bagadia, V. N. King Edward's Memorial Hospital, Bombay-12, India **Assessment of anatensol (Fluphenazine enanthate) injectable in the treatment of schizophrenia.** Bombay Hospital Journal (Bombay). 13(3):1-8, 1971.

Clinical descriptions and the various treatments for schizoprenia are discussed. Electroconvulsive therapy and pharmacological therapy are indicated as the best treatments for schizophrenia. Treatment with electroconvulsive therapy showed significant improvement in 90% of the patients. Pharmacological therapy is useful as concurrent and maintenance therapy; chlorpromazine and trifluoperazine being most widely used. Parental fluphenazine enanthate (Anatensol) is a potent neuroleptic but has limited use due to its side effects. Counseling and psychosurgery are also discussed. (Author abstract modified)

172741 Weston, M. J.; Bentley, R.; Unwin, A.; Morris, M.; Harper, M. A. University of Queensland, Clinical Sciences Building, Royal Brisbane Hospital, Brisbane, Queensland 4029, Australia **A comparative trial of haloperidol and thioridazine: management of chronic schizophrenia.** Australian and New Zealand Journal of Psychiatry (Carlton, Austrailia). 7(1):52-57, 1973.

The therapeutic effects of haloperidol and thioridazine on 86 hospitalized chronic schizophrenic patients are reported. The patients were randomly assigned to haloperidol and thioridazine groups and were treated following a flexible dosage, double-blind procedure for 12 weeks. Prior to the active drug regime, a 4 week period of placebo medication was initiated for all patients. The average daily dosage of thioridazine and haloperidol was 330mg and 5.3mg respectively. Each patient received anti-Parkinsonian medication in the form of orphenadrine hydrochloride. Prior to the administration of the psychotropic drugs and during the treatment period, all patients were rated on a symptom status and ward behavior rating scale. Patients receiving haloperidol tolerated the drug well and showed a significant degree of improvement on the rating scales. There appears to be no clinical evidence of any advantages in using thioridazine rather than haloperidol as a psychotropic agent when treating the chronic schizophrenic patient. 17 references. (Author abstract modified)

172831 Prien, Robert F.; Caffey, Eugene M., Jr.; Klett, C. James. Central Neuropsychiatric

Research Laboratory, VA Hospital, Perry Point, MD **Pharmacotherapy in chronic schizophrenia.** Washington, D.C., U.S. Government Printing Office, 1973. 20 p.

Maintenance chemotherapy of long-term schizophrenic illness is discussed, based on findings from selected studies and reviews. There is almost universal agreement that antipsychotic drugs are effective in treating schizophrenic behavior. After acute symptomatology subsides, the usual practice is to continue the patient indefinitely on medication. Only in recent years have clinicians begun to question the advisabilty of treating patients for long periods with antipsychotic drugs or to reemphasize the importance of other approaches in a program of truly active treatment of the chronically schizophrenic person. Some of the hazards and problems of long-term treatment with antipsychotic drugs are discussed. An overview of the use of antipsychotic drugs and a list of references dealing with major issues in extended treatment is also presented. 48 references. (Author abstract modified)

172963 Leff, J. P. Institute of Psychiatry, London, England **The maintenance treatment of schizophrenia.** Nursing Mirror and Midwives Journal (London). 137(10):26-27, 1973.

The drug maintenance treatment of schizophrenia is reported. Of a group of 116 patients, 20 were treated with Largactil and Stelazine, 15 were given placebos and 81 were not tested. All were followed up for a year. Relapse rate for Ss on drug use was 35%, for those on placebo 80%; maintenance therapy proved to be effective for acute schizophrenia. A long-term study of the treatment of chronic schizophrenics with Modecate was effective. Only 8% of the Ss relapsed while two thirds of those on placebo relapsed. Differences in schizophrenics and the effects of these differences on drug therapy are discussed. 4 references.

173402 Serafetinides, E. A.; Clark, M. L. Dept. of Psychiatry, University of California, School of Medicine, Los Angeles, CA **Psychological effects of single-dose antipsychotic medication.** Biological Psychiatry. 7(3):263-267, 1973.

Psychological effects of single dose antipsychotic medication are discussed. Effects of haloperidol (HAL), clopenthixol (CX), and chlorpromazine (CPZ) were studied at the beginning and end of a 12 week trial with schizophrenics. The aim was to correlate short-term and long-term effects and ascertain whether there was any indication for the use of single dose studies at baseline for the prediction of patient drug responses in the long run. As with longitudinal negative results, single dose studies showed few drug effects on psychological functions. Only the Purdue Pegborad (CPZ and CX) and the Dotting Test (HAL) registered some differences on the first trial. The Digit Symbol Test also showed changes as a result of chronic CPZ administration. Present findings indicate the hazardous nature of attempting to predict drug responses on the basis of such tests. 2 references.

173502 Lee, Won Yong; Moon, Hong Sei. National Mental Hospital, Korea **Psychological study on attitudes toward tranquilizers.** Neuropsychiatry (Seoul). 7(1):21-23, 1968.

Particular psychological motivations which may account for the attitude of drug evaders in Korean chronic hospitalized schizophrenic patients are discussed. Findings did not yield any particular constellation of attitude, although it is suggested that the drug evader is perhaps influenced by his negative attitude toward a coercive father image. It is concluded that the reasons and motivation of negative attitude in Korean patients toward the use of tranquilizers can be attributed to multiple factors in each individual. 3 references. (Author abstract modified)

173534 Karon, Bertram P.; VandenBos, Gary R. Michigan State University, East Lansing, MI 48823 **Medication and/or psychotherapy with schizophrenics: which part of the elephant have you touched?** East Lansing, Mi, Michigan State University, 1973. 22 p.

The relative effectiveness of psychotherapy, medication, and combined medication and psychotherapy as treatment for schizophrenic patients is discussed. The results of a study in which patients were assigned to the three forms of treatment are presented. It is concluded that medication is helpful but psychotherapy when reasonable care is taken in its implementation and in the training of the therapists, leads to even more benefits - particularly in the reduction of thought disorder and in the long-term consequences of that reduction on one's way of life. 14 references.

173563 Lee, Chung Kyoon. Department of Psychiatry, Medical College, Seoul National

University, Korea **Clinical study of thiothixene.** Neuropsychiatry (Seoul). 12(2):135-139, 1973.

Thiothixene treatment of nine schizophrenic patients is evaluated. Results indicate that the symptoms of emotional withdrawal, motor retardation, and blunted affect are improved by thiothixene treatment. Four of the nine patients showed moderate to severe extrapyramidal effects which were determined not to be serious. 10 references. (Author abstract modified)

174059 Davies, A. L; O'Leary, J. Neuropsychology and Research Unit, Friern Hospital, New Southgate, London, England **The use of chlorpromazine in schizophrenia.** Nursing Times (London). 69(12):1694-1695.

The procedure used in a series of experiments on the effects of chlorpromazine treatment on chronic schizophrenic inpatients is described. The clincal state of 20 male schizophrenics was manipulated by chlorpromazine therapy and later replaced by a placebo drug. A rating scale was developed to assess such factors as patient's social behavior, personal hygiene, mood, emotional, and intellectual state. Auditory selective attention and physiological tests were also administered during the drug and placebo phases. Chlorpromazine withdrawal led to deteriorated performance on the selective attention test. Physiological data revealed that heart rate, skin conductance and EEG patterns were distinctly different in the two phases of treatment. Overall, results demonstrate how a variety of measures change with the clincal state of a patient. These may be modified by a clinically useful drug, and through objective tests it should be possible to adjust the individual treatment according to individual needs.

174101 Kluge, H.; Hartmann., W.; Wieczorek, V.; Greger, J. Klinik fur Psychiatrie und Neuologie Hans Berger der Friedrich-Schiller-Universitat Jena, Philosophenweg 3, DDR-69, Jena /**Ongoing investigations of cerebral glutamin excretion schizophrenics during treatment with neuroleptic.**/ Verlaufsuntersuchungen zur zerebralen Glutamin ausscheidung bei schizophrenen unter Neuroleptikabehandlung Psychiatria Clinica (Basel). 6(5):288-299, 1973.

Studies of cerebral arteriovenous glutamine differences, carried out on 18 acute schizophrenics during special periods fixed by clinical parameters and dependent on medication, are discussed. Findings reveal that no differences were found in the acute phase without medication, but an increasing cerebral glutamine release is estimated under treatment with phenothiazine and/or butyrophenone derivatives during the first period of convalescence. Control persons treated in the same way did not show the cerebral glutamine release. A hypothesis is developed about disturbances in the ATP turnover and in the aminohydrolysis of AMP as ammonia source for the increased glutamine formation in schizophrenia. 16 references.

174131 Saletu, B.; Itil, T. M.; Arat, M.; Akpinar, S. Missouri Institute of Psychiatry, University of Missouri School of Medicine, St. Louis, MO **Long-term clinical and quantitative EEG effects of clopenthixol in schizophrenics: clinical-neurophysiological correlations.** International Pharmacopsychiatry (Basel). 8(4):193-207, 1973.

Long-term clinical and quantitative effects of clopenthixol in schizophrenics was studied. Evaluation of the overall clinical global impression ratings demonstrate a significant improvement during treatment as compared with the placebo period of treatment. Findings suggest that the number of significantly improved psychopathological items is greatest at the beginning of treatment, decreasing thereafter, reaching a minimum of 6 improved items in the sixth month, and increasing again at the end of therapy. Statistical analysis demonstrates a direct relationship between psychopathological and neurophysiological changes. 23 references. (Author abstract modified)

174134 Doust, John W. Lovett; Huszka, Louis; Little, M. Harvey. 250 College St., Toronto 2B, Canada **Metabolic control of body temperature in man.** International Pharmacopsychiatry (Basel). 8(4):239-244, 1973.

Metabolic control of body temperature in man is discussed. In a therapeutic trial of l-tryptophan in schizophrenia, adequate doses of a monoamine oxidase inhibitor (MAOI) and l-tryptophan were administered sequentially to seven human females, with the object of fostering the accumulation of predominantly noradrenalin in the brain by the former and exclusively of serotonin by the latter. Findings indicate that the MAOI drug alone produces a fall in body temperature, whereas the MAOI drug combined with l-tryptophan causes a rise in the majority of patients. 15 references. (Author abstract modified)

174137 Gallant, D. M.; Bishop, M. P.; Steele, C. A.; Bishop, G.; Guerrero-Figueroa, R. Tulane University School of Medicine, New Orleans, LA **Molindone: a crossover evaluation of capsule and tablet formulations in severely ill schizophrenic patients.** Current Therapeutic Research. 15(12):915-918, 1973.

A crossover evaluation of capsule and tablet formulations of molindone administered to severely ill schizophrenic patients is discussed. Findings confirm the previously established efficacy and safety of molindone in both capsule and tablet form. No suggestion of differential effect of the two preparations on side reactions was observed. It was further noted that patients suffer a consistent weight loss under both treatment conditions. 3 references. (Author abstract modified)

174587 Ramachandran, V.; Menon, M. Sarada. Madras Medical College, Madras-10, India **Trifluperidol - a controlled clinical trial on a group of schizophrenic patients.** Indian Journal of Psychiatry (Madurai). 14(1):11-18, 1972.

A double-blind controlled trial of trifluperiodol was undertaken by using 50 hospitalized schizophrenic patients. The trifluperidol and placebo groups were closely matched. A comprehensive psychiatric symptom rating scale, psychological tests and laboratory investigations, such as blood counts, liver profiles, and urine analysis, were employed to assess the improvement and side reactions of the drug. Eighty eight percent of the patients on trifluperidol showed marked improvement, while 8% showed moderate improvement. By contrast, only 8% and 28% of the patients on placebo showed marked and moderate improvement, respectively. Seventy two percent of the patients on trifluperidol exhibited extrapyramidal symptoms. Prophylactic antiparkinsonism drugs may be given. Laboratory investigations showed no significant pathological changes. 5 references. (Author abstract modified)

174588 Bagadia, V. N.; Jeste, D. V.; Chawla, R.; Shah, L. P.; Saraf, K. R. King Edward VII Memorial Hospital, Bombay-12, India **Trifluperidol in schizophrenia.** Indian Journal of Psychiatry (Madurai). 14(1):31-37, 1972.

The value and limitations of trifluperiodol in the treatment of schizophrenics were investigated. One hundred patients participated, with 76 completing 3 weeks or more of treatment. Significant improvement was observed in 65.8% of the patients. The highest rate of improvement was seen in cases of paranoid schizophrenia, in those with duration of illness less than 1 year, and in those with good and very good prognosis. Extrapyramidal system reactions were the commonest side-effects, and, in most cases, they responded to trihexyphenidyl hydrochloride. No serious side-effects were seen. 5 references. (Author abstract modified)

174589 Bagadia, V. N.; Shastri, P. C.; Dave, K. P.; Shah, L. P. Department of Psychiatry, K. E. M. Hospital, and Seth G. S. Medical College, Bombay-2, India **High doses of chlorpromazine and trifluoperazine in the treatment of patients suffering from schizophrenia.** Journal of Post Graduate Medicine (Bombay). 17(1):2-9, 1971.

The efficacy of chlorpromazine and trifluoperazine in the treatment of schizophrenia was compared. One hundred patients were divided into two equally matched groups. The matching was done on the basis of prognosis, which was determined by taking into consideration the type of schizophrenia, the duration of illness, the presickness personality, the type of onset and presence or absence of precipitating factors. Chlorpromazine produced an improvement rate of 68%; with trifluoperazine, 78%. The rapidity of improvement was almost equal. Excitment, insomnia, anorexia and thought disturbances remitted more frequently with chlorpromazine, whereas motor retardation, catatonic posture, apathy and emotional blunting remitted more frequently with trifluoperazine. Neither drug produced any serious side-effects. Extrapyramidal system side-effects were the commonest and were controlled easily by trihexyphenidyl. Other notable side-effects included giddiness and postural hypotension, dryness of mouth and nausea. Laboratory investigations showed no significant abnormality. 5 references. (Author abstract modified)

174680 Inui, Tadashi; Tanimukai, Hiroshi; Tanaka, Seiichi. Osaka University Department of Medicine, Osaka, Japan **Long-term application of clozapine (W-801) in schizophrenic patients.** Medical Consultation and New Remedies (Tokyo). 8(13):225-233, 1971.

The use of Clozapine, a benzodiazepine derivative, as an effective drug without extrapyramidal side-effects for use in the treatment of schizophrenic patients, is reported. Clozapine was used continuously for more than 1 year by eight

patients. The drug proved effective with all patients treated to date and has demonstrated dramatic effects on patient resistance. Patients are reported to have had transitory fevers, with accompanying increase in white corpuscle count, within 2 to 3 months after beginning with treatment by the drug, but no Parkinsonism was found. Differential blood count, liver functions, urine tests, blood pressure, body weight, and other factors, were normal after use for longer than 1 year. The results of extensive use of Clozapine indicate it to be a strong, but safe, drug, eminently effective in the treatment of schizophrenia. 6 references.

174681 Ishikawa, Hiroya. Saijo Mental Hospital, Japan **Clinical experiences with FK-880 (Sulpiride).** Medical Consultation and New Remedies (Tokyo). 9(10):2219-2227, 1972.

The results of clinical experience in the intramuscular injection of the neuroleptic Sulpiride are reported. Symptoms, age, sex, diagnosis, length of disease, whether hospitalized or outpatient, previous medication, dosage, additional medication used, change in symptoms, side-effects, and results are tabulated, as are urinalyses and blood pressures. Case histories of 18 schizophrenics show treatment to have been effective in one case, slightly effective in 10 cases, unchanged in six, and slightly worse in one. Of these patients, the drug was effective in five of six tension type cases (83%), in three of three behephrenic tension types (100%), and in three of nine hebephrenic types (33%). The drug was found to be quite effective for stupor, and substupor conditions, where refusal symptoms were evident, among those who talked to themselves, in unrest, depression, and anxiety. There were virtually no side-effects, and the safety factor was found to be high, and the drug was established as easy to use. 4 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

167344 Kline, N. S.; Shah, B. K. Rockland State Hospital, Orangeburg, NY **Comparable therapeutic efficacy of tryptophan and imipramine: average therapeutic ratings versus 'true' equivalence. An important difference.** Current Therapeutic Research. 15(7):484-487, 1973.

Therapeutic effects of tryptophan and imipramine were investigated. The efficacy or therapeutic equivalency of tryptophan is equal to that of imipramine. The study involved 34 Ss who were in the active depressive phase of their illnesses. 3 references. (Journal abstract modified)

167448 Kertesz, D.; de Korosy, F. Division of Chemistry, Negev Institute for Arid Zone Research, Beer Sheva, Israel **Effect of lithium on aggression, mania- and permselective membranes.** Experientia (Basel). 28(11):1338, 1972.

The possibility that the lithium ion has a strong effect on certain ion permselective membranes, which in some respects resemble neural membranes and may sometimes serve as their simplified model, was examined in an attempt to find the missing link in the explanation of the effect of lithium on aggressive and manic behavior. The possibility is suggested that Li+ increases the electric resistance of some nerve membranes, and that nerve membranes which become sluggish in their electrophysiological behavior ultimately also reduce more violent psychological effects. 20 references. (Author abstract modified)

167675 Dufour, H.; Schou, Mogens. no address **/Lithium in psychiatry./** Le lithium en psychiatrie. Encephale (Paris). 60(4):281-311, 1971.

Use of lithium in therapeutic psychiatry is analyzed in terms of its effects on manic-depressive psychoses during controlled and uncontrolled clinical tests. Nonpharmaceutical factors cause difficulty in evaluating quantitative effectiveness of the drug. Spontaneous remission is pointed out in particular. The treatment and prevention of manic and depressive relapses are presented in schematic form. Lithium pharmacology and toxicology are described and treatment outlined. Chemistry, absorption, and penetration into the cells as well as elimination, are detailed. The effectiveness of lithium to prevent relapses in cases of manic-depressive psychoses is noted. 72 references.

167774 Amin, M.; Brahm, E.; Bronheim, L. A.; Klingner, A.; Ban, T. A.; Lehmann, H. E. Div. of Psychopharmacology, McGill Univ., Montreal, P. Q., Canada **A double-blind, comparative clinical trial with Ludiomil (CIBA 34,276-Ba) and amitriptyline in newly admitted depressed patients.** Current Therapeutic Research. 15(10):691-699, 1973.

A double-blind clinical trial comparing Ludiomil (L), a tetracyclic dibenzobicyclo-octadiene, with amitriptyline (AT) was made. While there were no statistically significant differences in overall clini-

cal response to the drugs; more Ss responded favorably to L than to AT. Three out of four bipolar depressives showed hypomanic manifestations while on L. The possible significance of the finding is discussed. In one S a grand mal seizure was recorded with combined L and propoxyphene hydrochloride administration but there was no recurrence of cerebral seizures when propoxyphene was discontinued. 5 references. (Author abstract modified)

167775 Miller, William C., Jr.; Marcotte, David B.; McCurdy, Layton. Dept. of Psychiatry and Behavioral Sciences, Medical Univ. of South Carolina, Charleston, SC **A controlled study of single-dose administration of imipramine pamoate in endogenous depression.** Current Therapeutic Research. 15(10):700-706, 1973.

Thirty five clinic Ss with symptoms of depression, particularly of endogenous origin, were studied to compare once daily administration of a new pamoate salt of imipramine with three times per day administration of imipramine hydrochloride. Global depression, depression associated anxiety, neurotic symptoms and depressive symptomatology are evaluated. Study results confirmed the therapeutic equivalency between a single daily dose of imipramine pamoate and divided doses of imipramine hydrochloride. Mild side-effects occurred with equal frequency in both groups. 7 references. (Author abstract modified)

167917 Watanabe, Shosuke; Taguchi, Kanzo; Nakaya, Koji; Otsuki, Saburo. Department of Neuro-Psychiatry, Okayama University Medical School, Okayama, Japan **Clinical effects of lithium carbonate on depression.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 27(3):173-181, 1973.

The therapeutic effects of lithium carbonate were studied in 55 cases including involutional melancholia, monopolar depression, and bipolar depression. No significant differences in effectiveness are found among the three groups. No correlation between the characteristics of symptoms and the therapeutic effect in depressive states is observed. Lithium carbonate is effective in the treatment of depression but requires further study using the double-blind controlled method for clarification of its therapeutic effects. 21 references. (Author abstract modified)

167918 Watanabe, Shosuke; Taguchi, Kanzo; Nakaya, Koji; Noma, Takuji; Yokoyama, Shigeo; Otsuki, Saburo. Department of Neuro-Psychiatry, Okayama University Medical School, Okayama, Japan **Lithium carbonate treatment in manic psychosis.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 27(3):183-196, 1973.

The clinical effects of lithium carbonate on episodes of manic-depressive psychosis and schizoaffective psychosis were investigated. The effective rates of both manic episode and schizoaffective psychosis are moderate. The effect of lithium carbonate reaches its peak within 6 to 10 days of administration and its advantage is that its sedative effect is natural and not suppressive. Some gastrointestinal symptoms are seen as side-effects but do not hinder treatment. The results indicate that lithium carbonate is very effective for tranquilizing manic states and is clinically safe. 50 references. (Author abstract modified)

167919 Takahashi, Saburo; Kondo, Hisao; Yoshimura, Manabu; Ochi, Yukio; Yoshimi, Teruya. Department of Neurology and Psychiatry, Kyoto Prefectural University of Medicine, Kyoto, Japan **Growth hormone responses to administration of L-5-hydroxytryptophan (L-5-HTP) in manic-depressive psychoses.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 27(3):197-206, 1973.

Fourteen manic-depressive patients received L-5-hydroxytryptophan (L-5-HTP) to study the antidepressive effects and the human growth hormone (HGH) responses. Deficiency of pituitary HGH secretion appears to correlate neither with the score of Hamilton's Depression Scale nor with the judgement on the severity of illness, but may be due to a neurochemical defect hypothesized in the manic-depressive psychoses. The HGH responses were most distinctly diminished in the protracted depressive patients, suggesting an endocrine hypofunction which may cause the fixation of the depression symptoms. 24 references. (Author abstract)

168317 Ray, I. Department of Psychiatry, University Hospital, Saskatoon, Saskatchewan, Canada **Combinations of antidepressant drugs in the treatment of depressive illness.** Canadian Psychiatric Association Journal (Ottawa). 18(5):399-402, 1973.

Seventy three inpatients and 11 outpatients, aged 16-76, were treated with modified sleep, combined antidepressant drugs and ECT. Every patient had treatment with psychotropic drugs

prior to referral to the Yorkton Psychiatric Centre. Sideeeffects encountered during the treatment were minimal. Concomitant ECT was also used with combined antidepressant drugs, and recovery of all patients from anesthesia during ECT was uneventful. Results of treatment of global assessment showed considerable improvement in 52 patients, 30 improved, and no change in two patients. The average stay in the hospital was 19.5days. 16 references. (Author abstract)

168318 McClure, D. J.; Low, G. L.; Gent, M. Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Clomipramine HCL--a double-blind study of a new antidepressant drug.** Canadian Psychiatric Association Journal (Ottawa). 18(5):403-408, 1973.

A double-blind study was carried out comparing the antidepressant and anxiolytic properties of clomipramine HCL (a new antidepressant) and imipramine on a group of 24 subjects suffering from psychotic depression. The patients were divided into two groups of twelve by random sampling. Clinical assessments were made by two independent psychiatrists and a psychologist. Clomipramine HCL was found to be as effective as imipramine in the treatment of depression, and it also showed similar anxiolytic properties. There were no significant changes in the laboratory tests carried out before and after the treatment program was completed in both treatment groups. 9 references. (Author abstract modified)

169087 Klerman, Gerald; DiMascio, Alberto. Massachusetts Department of Mental Health, Boston, MA **Long-term treatment of depression with drugs and psychotherapy.** Psychopharmacology Bulletin. 9(4):55, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, an examination of the relative effectiveness of drugs and psychotherapy in the maintenance treatment of 150 depressed women who had responded to pharmacotherapy with amitriptyline was discussed. The subjects were treated for an 8 month period using a six cell design (amitriptyline, placebo, or no pill, with and without individual psychotherapy). The results showed that there was a significant further improvement over the study time on the patients' self-assessment but not on the psychiatrist's ratings for those patients who were continued on the active medication regardless of whether they were in psychotherapy or not. The relapse rates indicate that psychotherapy did not enhance the effects of administering a medication to help prevent a relapse. (Journal abstract modified)

169088 Friedman, Alfred S. Philadelphia Psychiatric Center, Philadelphia, PA **Drug therapy and marital therapy in outpatient depressives.** Psychopharmacology Bulletin. 9(4):55-57, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the effects of a tricyclic antidepressant, amitriptyline, alone and in combination with marital therapy in the outpatient treatment of depressed patients in the acute phase of depression was examined. The drug effects were superior to the marital therapy effects in regard to improvement in the patient's symptomatic and clinical condition. But the marital therapy effects were superior to the drug effects in regard to improvement in the patient's participation and performance in the family role tasks. It is suggested that both types of outcome and improvement are essential. 2 references. (Journal abstract modified)

169090 Prien, Robert F. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD **A comparison of lithium carbonate in the prevention of manic and depressive episodes in recurrent affective disorder.** Psychopharmacology Bulletin. 9(4):59, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, 130 patients with recurrent affective illness in 16 hospitals who were randomly assigned to lithium carbonate, imipramine, or placebo following discharge from hospitalization for acute depression (with or without manic episodes) were examined. The results emphasize the importance of considering the patient's previous course of illness before selecting a program of maintenance chemotherapy. Patients with a history of manic episodes (bipolar patients) are not good candidates for a program involving imipramine. The risk of subsequent manic attack is too great. Lithium carbonate is a more suitable treatment for these patients. Patients with a history of depression without mania (unipolar patients) may be treated effectively with either lithium carbonate or imipramine. (Journal abstract modified)

169092 Shagass, Charles. Dept. of Psychiatry, Temple University, Philadelphia, PA 19122

Changes in somatosensory evoked potentials produced by drugs used in the treatment of affective disorders. Psychopharmacology Bulletin. 9(4):61-62, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the changes in somatosensory evoked potentials produced by lithium carbonate and amitriptyline in the treatment of 14 patients with the affective disorders of hypomania, mania, or schizoaffective syndrome was discussed. The results indicate that lithium carbonate and amitriptyline had different effects on the evoked potential measures of central excitability. Some consideration is given to the possible relationship of these findings to the opposite effects of these drugs on central norepinephrine availability. It is suggested that if there is any connection between the evoked potential changes demonstrated and catecholamine activity, it would be necessary to assume that increased available norepinephrine produces greater inhibitory activity. This would account for the evoked potential amplitude reductions produced by amitriptyline and increases effected by lithium. 2 references. (Journal abstract modified)

169093 Mendels, J. Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **The heterogeneity of depression.** Psychopharmacology Bulletin. 9(4):62-64, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, studies extending over 8 years and directed towards the discrimination between subtypes of depression and the response to different treatment modalities on the one hand and clinical symptomatology and particular biological observations on the other hand were briefly summarized. The data suggest the possibility that the erythrocyte may serve as a model for the study of lithium (and perhaps other drugs) in psychiatric patients. The findings also suggest that there may be a significant difference in the way lithium is being handled by depressed patients who do and depressed patients who do not respond to lithium treatment. It is suggested that the data have important implications for both the treatment of depressed patients with lithium carbonate as well as the providing of a potential new strategy for research studies. 12 references. (Journal abstract modified)

169094 Shopsin, Baron. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, New York, NY **A collaborative assessment of norepinephrine metabolism in affective disorders.** Psychopharmacology Bulletin. 9(4):64-65, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, a review of five collaborative studies which cannot support any theory of disturbed norepinephrine metabolism as specific for the affective disorders of mania or depression was related. Because these investigations question the catecholamine hypothesis, it is suggested that (1) new directives be sought to develop newer and more sensitive methods with which to detect any aberrant changes in the metabolism of catecholamines in affective illnesses and (2) investigations into other areas of possible relevance other than amines be stimulated. 5 references. (Journal abstract modified)

169095 van Praag, H. M. Dept. of Biological Psychiatry, Psychiatric University Clinic, Groningen, The Netherlands **Towards a biochemical typology of depression.** Psychopharmacology Bulletin. 9(4):65-66, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology two arguments that support the theory that in humans as in test animals, the probenecid technique supplies valid information on the central turnover of 5-hydroxytryptamine (5-HT) and dopamine in depressed patients were discussed. The 5-hydroxyindoleacetic acid response to probenecid is diminished in depressive patients. This phenomenon was more pronounced in the group of endogenous depressions than in that of neurotic depressions. Assuming the probenecid technique to be valid in humans, these findings support the hypothesis which postulates a correlation between cerebral 5-HT deficiency and the occurrence of depressive symptoms. After probenecid, depressive patients showed a less marked increase in the cerebrospinal fluid homovanillic acid concentrations that controls. This fact supports hypotheses which postulate a correlation between disturbances in the central catecholamine metabolism and the occurrence of depressive symptoms. 8 references. (Journal abstract modified)

169296 Ban, Thomas A. Div. of Psychopharmacology, McGill University, Montreal, Quebec, Canada **Haloperidol and the butyrophenones.** Psychosomatics. 14(5):286-297, 1973.

A review of the psychopharmacological implications of haloperidol and the butyrophenones is presented. From a practical point of view, it is important to know that haloperidol is one of the best available drugs in the control of psychopathological symptoms in mania. From a theoretical point of view, however, more important are the findings in Gilles de la Torette's disease, possibly in obsessive compulsive neurosis and schizophrenia. The finding that haloperidol exerts central and antiadrenergic effects with virtually no central anticholinergic action may explain the relatively low incidence of autonomic adverse effects with this drug. 124 references.

169468 Eisenring, J. J.; Dick, P.; Tissot, R.; Yanniotis, G. Clinique Psychiatrique de l'Universite, Bel-Air pres Geneve, CH-1225 Chene-Bourg, Suisse **/Combination of L-Dopa, desipramine, and a decarboxylase inhibitor in the treatment of depression./** Association L-Dopa, desipramine et inhibiteur de la decarboxylase dans le traitement de la depression. Psychopharmacologia (Berlin). 33(1):95-101, 1973.

A combination of L-Dopa, a decarboxylase inhibitor, and desipramine was used in depressed patients. Some types of depression were rapidly relieved by such treatment, while those types associated with anxiety and agitation did not respond. 20 references. (Author abstract modified)

169491 Mendels, J.; Digiacomo, Joseph. Depression Research Unit, University of Pennsylvania, Philadelphia, PA 19104 **The treatment of depression with a single daily dose of imipramine pamoate.** American Journal of Psychiatry. 130(9):1022-1024, 1973.

A controlled comparison of the effects of 50mg of imipramine hydrochloride given three times daily and 150mg of imipramine pamoate in a single bedtime dose to depressed patients is reported. Results revealed no significant difference in either therapeutic effects or side-effects in the group of 40 hospitalized depressed patients. The advantages of a single night dose of antidepressant medication are discussed. 4 references. (Author abstract modified)

169494 Mendlewicz, Julien; Fieve, Ronald R.; Stallone, Frank. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Relationship between the effectiveness of lithium therapy and family history.** American Journal of Psychiatry. 130(9):1011-1013, 1973.

The relationship between the effectiveness of lithium therapy and family history was studied. Seventy two manic-depressive patients were randomly assigned to treatment with either lithium carbonate or placebo. Of these, 67% were treated successfully and 33% were long-term failures. Data that reflected the incidence of psychopathology in the first and second degree relatives of the patients were collected. Striking differences were observed in the backgrounds of lithium responders and failures: response to lithium treatment was significantly associated with the presence of manic-depressive illness in the patients' families. 15 references. (Author abstract)

169495 Stallone, Frank; Shelley, Edward; Mendlewicz, Julien; Fieve, Ronald R. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **The use of lithium in affective disorders, III: a double-blind study of prophylaxis in bipolar illness.** American Journal of Psychiatry. 130(9):1006-1010, 1973.

The use of lithium in affective disorders was examined in a double-blind study of prophylaxis in bipolar illness. Fifty two manic-depressive patients were assigned to either lithium or placebo during their normal interval phases for periods up to 28 months. Patients receiving lithium had fewer manic and depressive episodes per patient year than placebo patients. It is suggested that this difference may have been due to a sample bias produced by a large dropout rate among patients who had manic episodes. The findings suggest a relationship between response to lithium and family history of bipolar illness. 12 references. (Author abstract modified)

169504 Henry, George M.; Weingartner, Herbert; Murphy, Dennis L. Department of Psychiatry, University of Kentucky College of Medicine, Lexington, KY 40506 **Influence of affective states and psychoactive drugs on verbal learning and memory.** American Journal of Psychiatry. 130(9):966-971, 1973.

The influence of affective states and psychoactive drugs on verbal learning and memory were studied. Evidence of impaired performance on

serial and free recall verbal learning tasks during depression and mania is presented. Treatment with L-dopa and L-tryptophan significantly improved performance on these tasks, while imipramine, lithium carbonate, and alpha-methyl-para-tyrosine treatments had no effect. These results should be taken into account when using psychotherapeutic approaches designed to teach new response patterns to patients with affective disorders. 47 references. (Author abstract modified)

170079 Greenwood, Laurence; Goodwin, Frederick K. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Drugs and psychodynamic shifts in affective illness. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 13 p.

Case study material is presented on the effects of pharmacological drugs on the psychodynamic function of patients suffering from affective disorders, such as depression and mania. Data indicate that prolonged unfulfilling intimate features are often present in such persons, and the mechanism of 'negative insight' exists for ignoring the internal and external realities of the situation. The manic-depressive patient communicates both verbally and by the tone and tempo of his behavior a different message in each phase of his illness. Two supplementary hypotheses regarding the functioning of drugs in treatment of such patients are given: 1) drugs diminish the affective psychobiological impact which losses or added burdens create, and the patient is not so threatened with having to face his life situation and can return to euthymia; and 2) the drug makes it difficult for the patient to continue expanding energy in the style which is required to maintain the manic or depressive position. 24 references. (Author abstract modified)

170084 Goodwin, Frederick K.; Post, Robert M. NIMH, Bethesda, MD 20014 **Brain serotonin, affective illness and antidepressant drugs: cerebrospinal fluid studies with probenecid. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 13 p.

Alterations in the probenecid induced accumulation of 5-hydroxyindoleacetic acid (5-HIAA), the major metabolite of serotonin, produced by a serotonin precursor and synthesis inhibitor were examined to provide evidence for the validity of this technique in estimating CNS serotonin turnover. Differences in the probenecid induced accumulation of 5-HIAA were examined in normal controls, and in patients with affective illness divided according to diagnostic groups, severity of various symptoms, and response to treatment. Finally, two tricyclic antidepressants (imipramine, IMI, and amitriptyline, AMI) were examined for their effects on the probenecid induced accumulation of 5-HIAA. Data are similar with other reports on probenecid. Results with the tricyclic drugs suggested that CNS turnover of 5-HT is reduced during treatment with these antidepressants. The technique provides a useful tool for directly assessing central amine neurotransmitter turnover in patients, and as such, appears to reflect a presynaptic function. 52 references.

170621 Kotin, Joel; Post, Robert M.; Goodwin, Frederick K. Department of Psychiatry and Human Behavior, University of California at Irvine, Irvine, CA **Drug treatment of depressed patients referred for hospitalization.** American Journal of Psychiatry. 130(10):1139-1141, 1973.

The clinical impression that many depressed patients are admitted to hospitals without having received adequate drug treatment as outpatients was confirmed with a sample of 51 depressed patients. Of these, only 20% had received proper drug treatment before referral. A larger study of the actual patterns of drug prescription is proposed to seek the causes of inadequate treatment. 6 references. (Journal abstract modified)

170622 Hussain, M. Z.; Chaudhry, Z. A. Psychiatric Centre, Victoria Union Hospital, 1200-24th Street West, Prince Albert, Saskatchewan, Canada **Single versus divided daily dose of trimipramine in the treatment of depressive illness.** American Journal of Psychiatry. 130(10):1142-1144, 1973.

A group of 56 patients with depressive illnesses were administered either a single daily dose or a divided daily dose of trimipramine on a random basis. Results of treatment showed several advantages for the use of a single daily dose: a trend toward better therapeutic improvement, a significant decrease in the side-effects of insomnia and fatigue, and more regular consumption of the medication. Dosage should be 150mg. or more, as smaller doses are probably too low to have much therapeutic effect. 15 references. (Author abstract modified)

170627 SanGiovanni, Francine; Taylor, Michael A.; Abrams, Richard; Gaztanaga, Pedro. Depart-

ment of Psychiatry, New York Medical College, Metropolitan Hospital Center, 1901 First Ave., New York, NY 10029 **Rapid control of psychotic excitement states with intramuscular haloperidol.** American Journal of Psychiatry. 130(10):1155-1156, 1973.

An open clinical trial of high doses of parenteral haloperidol in the treatment of 40 acutely excited psychotic inpatients was conducted. Preliminary results suggest that intramuscular haloperidol in doses up to 60mg/day is safe, effective, and well tolerated in the management of such patients. Adverse reactions, which were infrequent, included extrapyramidal symptoms, lethargy, and, in one patient, transient hypotension. 4 references. (Journal abstract modified)

171161 Prijosembodo, Wartomo. Department of Psychiatry, School of Medicine, University of Indonesia, Salemba 6, Djakarta, Indonesia **Clinical trial of trifluoperazine (Stelazine R) on Indonesian psychiatric patients.** Indonesian Psychiatric Quarterly (Djakarta). 5(4):81-91, 1972.

Data on the usefulness of trifluoperazine (Stelazine) on psychiatric patients was studied in terms of local needs, situations and subjects. More than 85% of the symptomatology shows improvement with Stelazine treatment. Symptoms of acute psychosis seem to respond well to Stelazine treatment. Many side-effects were encountered but in general they can be controlled by antiparkinson drugs. This clinical trial has shown that Stelazine is indeed a potent drug for the treatment of a variety of psychotic conditions especially for the Indonesian patient belonging to the Javanese ethnologic group.

171500 Prange, Arthur J., Jr.; Wilson, Ian C.; Lynn, Clabe W.; Alltop, Lacoe B.; Stikeleather, Rachel A. Department of Psychiatry, School of Medicine, Univ. of North Carolina, Chapel Hill, NC 27514 **L-Tryptophan in mania: contribution to a permissive hypothesis of affective disorders.** Archives of General Psychiatry. 30(1):56-62, 1974.

Five manic patients treated with chlorpromazine hydrochloride (CPZ), then with L-tryptophan (LTP), and five with LTP first, then CPZ, in a double-blind, placebo controlled crossover study were assessed. The Sainsbury scale and the Inpatient Multidimensional Psychiatric Scale were utilized to judge treatment effectiveness. LTP was slightly superior to CPZ in all regards. Mania and depression may be linked by a central indoleamine deficit. 50 references. (Author abstract)

171501 Ehrensing, Rudolph H.; Kastin, Abba J. Dept. of Psychiatry and Biobehavioral Sciences, Louisiana State Univ. Medical Center, 1542 Tulane Ave., New Orleans, LA 70112 **Melanocyte-stimulating hormone-release inhibiting hormone as an antidepressant: a pilot study.** Archives of General Psychiatry. 30(1):63-65, 1974.

The melanocyte - stimulating hormone (MSH) release inhibiting hormone, prolyl-leucyl-glycinamide (MRIH-I), a hypothalamic hormone, active in animal systems used as models of depression, was tested in humans. In a double-blind, clinical trial, four of five patients with mental depression, who received 60mg of MRIH-I for each of 6 consecutive days, experienced marked improvement for their symptoms within 2 to 3 days. The preliminary nature of these findings, however, is emphasized by the improvement in two of four patients receiving a placebo and only two of five patients receiving 150mg of MRIH-I. 15 references. (Author abstract)

171502 Raskin, Allen; Schulterbrandt, Joy G.; Reatig, Natalie; Crook, Thomas H.; Odle, David. Rm 9-101 NIMH, 5600 Fishers Lane, Rockville, MD 20852 **Depression subtypes and response to phenelzine, diazepam, and a placebo: results of a nine hospital collaborative study.** Archives of General Psychiatry. 30(1):66-75, 1974.

A total of 325, newly admitted, depressed patients from nine hospitals randomly assigned to treatment with either diazepam, phenelzine, or a placebo were evaluated. The study was conducted double-blind and ran for 7 weeks. Median daily dosages were 30mg of diazepam and 45mg of phenelzine. The major finding was the differential effects of diazepam for patients categorized as anxious and hostile depressions. There was a significant number of anxious - depressive patients who were diazepam responders, their symptoms subsided on this treatment and became worse when this drug was discontinued. In contrast, diazepam was a poor treatment for the hostile depressions. These patients were restless, anxious, negativistic, suspicious, and irritable when they entered the study. These symptoms persisted on diazepam and improved on either phenelzine or a placebo. 62 references. (Author abstract)

171503 Kupfer, David J.; Reynolds, Charles F., III.; Weiss, Brian L.; Foster, F. Gordon. Dept. of Psychiatry, Univ. of Pittsburgh School of Medicine, Western Psychiatric Instit. and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Lithium**

carbonate and sleep in affective disorders: further considerations. Archives of General Psychiatry. 30(1):79-84, 1974.

The effect of lithium carbonate on electroencephalographic sleep parameters was evaluated in six patients with affective disorders. Confirming earlier results, significant reductions in rapid eye movement (REM) percent and phasic-REM activity during the drug period is reported. Doubling of delta-sleep time occurred during lithium administration, and a negative correlation between REM percent and delta percent was found; there was no immediate REM compensation in the postdrug period. We propose a model for REM suppression based on REM-cycle length and the presence or absence of REM rebound. 17 references. (Author abstract)

171695 Abuzzahab, F. S., Sr. Department of Psychiatry, University of Minnesota, Minneapolis, MN 55455 **A double blind investigation of dimethacrine versus imipramine in hospitalized depressive states.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 8(3):244-253, 1973.

In a 4 week double-blind investigation in depressed inpatients, dimethacrine was found to be less effective than imipramine as an antidepressant. No evidence of a relatively more rapid onset of action was obtained. Dimethacrine had less sedative action, fewer anticholinergic effects and produced more alterations in liver functions than imipramine. 24 references. (Author abstract)

171923 Raskin, Allen. Psychopharmacology Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20852 **A guide for drug use in depressive disorders.** American Journal of Psychiatry. 131(2):181-185, 1974.

Information from the multihospital NIMH collaborative studies of drugs and depression that might be of practical use to the clinician is presented. The drugs used in these controlled studies were chlorpromazine, imipramine, diazepam, and phenelzine, drugs that exert different effects on the major symptoms of depression and on certain patient subtypes. The frequency and nature of adverse reactions to these drugs are described. 42 references. (Author abstract)

171926 Prien, Robert F.; Klett, C. James; Caffey, Eugene M., Jr. Central Neuropsychiatric Research La[illegible]tory, Veterans Administration Hospital, Per[illegible] Point, MD 21902 **Lithium prophylaxis in recurrent affective illness.** American Journal of Psychiatry. 131(2):198-203, 1974.

The effectiveness of lithium carbonate in treating recurrent affective illness was studied. In study I, 205 bipolar (manic-depressive) patients were randomly assigned to lithium or placebo; in study II, 44 bipolar and 78 unipolar (depressive) patients were randomly assigned lithium, imipramine, or placebo. The results showed lithium to be effective in treating both manic and depressive episodes and imipramine to be effective in treating depressive episodes. The findings emphasize the importance of considering the patient's previous course of illness in selecting a program of maintenance treatment. 18 references. (Author abstract)

172401 Persson, G. Department of Psychiatry, Sahlgrens Hospital, 413 45 Gothenburg, Sweden **Lithium prophylaxis in affective disorders: an open trial with matched controls.** Acta Psychiatrica Scandinavica (Kobenhavn). 48(6):462-479, 1972.

Patients with bipolar and unipolar affective psychoses were given lithium prophylaxis, and the course of disease during 2 years was compared with matched nonlithium patients from the same clinic but from an earlier period. Periods of both 1 and 6 months were used. Measures of disease include relapse or not, number of relapses, average duration of disease, treatment as inpatients, number of days spent in hospital, and treatment with ECT. Among unipolar patients, almost all comparisons were in favor of lithium; among bipolar patients with 1 month intervals most comparisons were in favor of lithium; among those with 6 months intervals, there were tendencies in the same direction. At least for unipolar patients it seems probable that lithium can stabilize a treatment induced remission and prevent the onset of new episodes. 11 references. (Author abstract modified)

172402 Bjorum, N.; Plenge, P.; Rafaelsen, O. J. Department of Psychiatry, Frederiksberg Hospital, 57, Ndr. Fasanvej, 2000 Copenhagen F, Denmark **Electrolytes in cerebrospinal fluid in endogenous depression.** Acta Psychiatrica Scandinavica (Kobenhavn). 48(6):533-539, 1972.

Electrolytes in cerebrospinal fluid were determined in 21 patients before and after recovery from endogenous depression. Inorganic phosphate

was significantly higher in depressed patients than in controls and increased further during recovery. 13 references. (Author abstract)

172976 Korn, M. no address **/Our experience with lithium./** Notre experience du lithium. Feuillets Psychiatriques de Liege (Liege). 5(2):206-211, 1972.

Results of a 2 year experiment in treating 20 manic-depressive patients between the ages of 22 and 66, hospitalized for from 1 month to 20 years, with lithium are detailed. Nine cases appeared to stabilize, eight cases were stopped, one by suicide. Two cases were treated so briefly that results are inconclusive. It is concluded that lithium treatment for manic-depressive cases shows slight success whether administered alone or in combination with other drugs. Lithium may have a place with the neuroleptics, but currently is considered to be of little use as a substitute for classic medications. 7 references.

172978 Brasseur, R. no address **/Preliminary study of the treatment of chronic psychoses with flupenthixol decanoate./** Etude preliminaire concernant le traitement des psychoses chroniques par le decanoate de flupenthixol. Schweizerische Rundschau fur Medizin. No. 60:1107-1113, 1971.

Results of a preliminary study of 20 chronically psychotic patients by flupenthixol in decanoic ester form are discussed. The drug is described as a neuroleptic with long-term kinetic action. Patients treated in the study averaged 34 years of age, and were of both sexes. The drug had rapid and favorable effects in some cases, drug was ineffective in cases of chronic delirium when evaluated on an interpretive base. The effect on anxiety is not discussed.

172979 Brasseur, R. no address **/Clinical experience with melithracene in the treatment of depressive states./** Experience clinique avec le melithracene dans le traitement des etats depressifs. Schweizerische Rundschau fur Medizin. No. 60:249-253, 1971.

The results of a clinical experiment in the use of melithracene (Dixeran), a drug with a chemical structure similar to that of dimethacrine (Istonil), to treat psychic and psychomotor inhibition, melancholia, and abulia are described. Dosages and results are collated and facts are correlated with cerebral electrogenesis. Tremors, slight akathisia, and a minor sign of the cogwheel effect were observed when the dosage was above 150mg.

173006 Chien, Ching-Piao; Dimascio, Alberto; Cole, Jonathan O. Department of Psychiatry, Tufts University School of Medicine, Boston, MA **Antiparkinsonian agents and depot phenothiazine.** American Journal of Psychiatry. 131(1):86-90, 1974.

To determine whether antiparkinsonian (AP) drugs should be regularly given prophylactically to all patients receiving depot antipsychotic drugs, 41 psychotic patients receiving fluphenazine enanthate were assigned to one of three groups. The first received only enough AP medication to control the occurrence of acute extrapyramidal symptoms (EPS), the second received AP medication for 5 days after each injection of depot fluphenazine, and the third received the AP agent daily. There were no significant differences among the three groups in the number and intensity of EPS, although some subjects in the first group displayed gross EPS that were controlled. It is concluded that the routine prophylactic use of AP drugs is questionable but that further research is necessary. 12 references. (Author abstract)

173520 Richardson, J. Steven; Lamprecht, Friedhelm. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Cholinergic reversal of manic symptoms: a possible explanation. (Unpublished paper).** Bethesda, MD, NIMH, 1973, 3 p.

A possible explanation of cholinergic reversal of manic symptoms was presented. Shortly after intravenous injection of physostigmine into rats, tyrosine hydroxylase (TH) activity in the hypothalamus is decreased. The effect of physostigmine on TH activity was not blocked by atropine. It is unlikely that physostigmine or a metabolite has a direct action on TH. Cholinergic activation by the irreversible acetylcholinesterase inhibitor diisopropylflurophosphate also produces a 20% decrease in TH activity after intraperitoneal injection. However, 15 minutes after cholinergic activation by carbachol, TH activity was unaltered. While the mechanism for the transient decrease in TH activity shortly after administration of physostigmine is unknown, this action could explain the rapid transient improvement of manic patients treated with intravenously applied physostigmine. 2 references.

174093 Dunner, David L.; Fieve, Ronald R. New York State Psychiatric Institute, 722 W. 168th

Street, New York, NY 10032 **Clinical factors in lithium carbonate prophylaxis failure.** Archives of General Psychiatry. 30(2):229-233, 1974.

Failure to prevent the recurrence of manic or depressive episodes was observed in 27 to 55 bipolar (manic-depressive) patients who received lithium carbonate for from 6 to 66 months. Several clinical features of these patients were examined to determine if any predicted lithium carbonate prophylaxis failure. Patients whose frequency of affective episodes was at least four per year (rapid cyclers) were disproportionally represented in the prophylaxis failure group. For the nonrapid cyclers, prophylaxis failure occurred mainly in the first year of lithium carbonate treatment and tended to be characterized by more than one affective episode. Most of the rapid cyclers continued to be ill even after 2 years or more of lithium carbonate treatment, although some beneficial effects of lithium carbonate could be demonstrated in the rapid cycler group. 13 references. (Author abstract)

174094 Post, Robert M.; Goodwin, Frederick K. 3-West Unit, Adult Psychiatry Branch, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20014 **Effects of amitriptyline and imipramine on amine metabolites in the cerebrospinal fluid of depressed patients.** Archives of General Psychiatry. 30(2):234-239, 1974.

The effect of tricyclic antidepressant treatment on the metabolism of brain serotonin and dopamine was evaluated in depressed patients by studying levels of the respective metabolites (5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA)) in the cerebrospinal fluid (CSF) after the administration of probenecid. Probenecid caused rapid accumulation of 5-HIAA and HVA by inhibiting transport out of the CSF, thus providing a measure of amine turnover. Treatment with amitriptyline hydrochloride and imipramine hydrochloride was associated with a reduced accumulation of 5-HIAA, whereas, HVA accumulation was not affected. These findings suggest that, in depressed patients, central nervous system serotonin turnover is decreased during treatment with amitriptyline and imipramine. 58 references. (Author abstract)

174136 Krueger, G. A. W. 2000 Hamburg 70, Nordschleswiger Strasse 5, Germany **Use of lorazepam in treating patients with neurotic and somatized psychovegetative symptoms.** Current Therapeutic Research. 15(12):907-914, 1973.

Use of lorazepam in treating patients with neurotic and somatized psychovegetative symptoms are discussed. Findings indicate that the therapeutic response to lorazepam is excellent. Side-effects are minimal and easily managed. Results suggest no clinically significant changes in patients with a history of liver, kidney, or endocrine disease. 14 references. (Author abstract modified)

174138 Sathananthan, G. L.; Matz, R.; Thompson, H.; Gershon, S. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Amoxapine and imipramine: a double-blind study in depressed patients.** Current Therapeutic Research. 15(12):919-922, 1973.

The effects of amoxapine and imipramine were evaluated in a double-blind study with depressed patients. Findings suggest that amoxapine might be useful as an antidepressant drug. Contingency factors which might have affected the outcome of the study are discussed, and results summarized. 6 references. (Author abstract modified)

174299 Olgiati, Sandro; Calobrisi, Arcangelo. Dept. of Psychiatry, Knickerbocker Hospital, New York, NY **Clinical results with pizotyline in depression.** Diseases of the Nervous System. 35(1):35-38, 1974.

Clinical results with pizotyline in depression are investigated. Pizotyline at two dosage levels, or one dosage level of amitriptyline, was administered under double-blind conditions to 100 depressed outpatients in a community mental health clinic; 73 patients completed the 4-week study. Statistical analyses of the results showed one significant difference among the three treatment groups' responses: sleep disturbance decreased significantly more in patients receiving the higher pizotyline dosage. The three treatment groups' responses measured by the other rating scale items did not differ significantly. Ten of the 75 patients taking pizotyline and four of the 25 patients taking amitriptyline developed side-effects. It is concluded that to clarify dose and time related variables, additional studies are required. 10 references. (Author abstract modified)

174329 Goodwin, Frederick K.; Sack, Robert L. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD **Behavioral effects of a new dopamine-beta-hydroxylase inhibitor (fusaric acid) in man. (Unpublished paper)** Rockville, Md., NIMH, 1974. 17 p.

Results of a clinical trial of fusaric acid in patients with primary affective disorders were reported. Fusaric acid was administered under double-blind conditions to nine patients at an average maximum daily dose of 1.12 grams for a total period of 10 to 20 days. Fusaric acid was well tolerated with a minimal effect on blood pressure and no alteration in indices of hepatic, hematologic, renal or endocrine function. The effects of fusaric acid appeared to depend on the preexisting clinical state. Patients with Stage III mania or with evidence of preexisting psychotic features became consistently worse - that is, more psychotic; however, a few patients with mild hypomanic symptoms showed slight improvement in ratings. 34 references.

174376 Teja, Jagdish S.; Bhatia, S. C. University of Virginia School of Medicine, Charlottesville, VA **A double blind trial of iprindole and imipramine in depressives and response to E.C.T. in refractory cases.** Indian Journal of Psychiatry (Madurai). 14(1):1-10, 1972.

Iprindole, an antidepressant of the tricyclic group, is assessed as to potency, onset of action, and side-effects, compared to imipramine hydrochloride. In 65 cases of functional depressive illness, the results of double-blind studies indicate that iprindole in smaller dosages is more effective than imipramine, with less severe side-effects. Patients responding poorly to either drug were administered electroconvulsive therapy (ECT), 80% showing good improvement. 7 references. (Author abstract modified)

174566 Billings, Edward G. no address **Electroencephalographic modifications during administration of lithium.** Rocky Mountain Medical Journal. 71(2):99-103, 1974.

Electroencephalographic (EEG) modifications during prolonged administration of lithium carbonate to patients long given to recurring affective reactions are discussed. Twenty two affectively sick patients, 18 women and four men, aged 20 to 74 years, are studied. No double-blind therapeutic test or control group studies were accomplished. Four case studies are examined individually. It is problematical whether the typical EEG changes that occur in some patients incident to lithium administration may constitute clues as to why therapeutic improvement occurs or are reflections of toxic effects of the lithium ion. Results show that there is no commonly accepted mechanism by which lithium is thought to exert its thereapeutic effects in these disorders. 13 references.

174778 Rybakowski, Janusz; Hernacka, Barbara; Kapelski, Zdzislaw. Klinika Psychiatryczna AM, ul. Szpitalna 27/33, Poznan, Poland **/Long-term use of lithium carbonate in affective disorders: a clinical evaluation./** Ocena kliniczna dlugotrwalego podawania weglanu litu chorym z zaburzeniami afektywnymi. Psychiatria Polska (Warszawa). 7(2):179-183, 1973.

Results of long-term use of lithium carbonate in treating 28 patients with cyclophrenia and unipolar depression are discussed and tabulated. The course of the illness was studied in each patient over periods of equal length prior to and during administration of the drug. The number of hospitalizations are shown to have decreased, and clinical symptoms were alleviated markedly. Side-effects were manageable in the majority of cases with no need to interrupt treatment. The question of the influence of lithium on the length of the morbid cycle will require further study. 8 references. (Author abstract modified)

174851 Jha, B. K. Hospital for Mental Diseases, Kanke, Ranchi-6, Bihar, India **Antidepressant drugs.** Journal of Clinical Psychi-7). 1(1):47-63, 1973.

Major classes of antidepressant drugs are surveyed in terms of pharmacological action, suggested dosages and side-effects. General guidelines for selecting tricyclic antidepressants or monoamine oxidase inhibitors are presented and rules for changing drugs are reviewed. 34 references.

10 DRUG TRIALS IN NEUROSES

167339 Feurst, Samuel I. Martin-Feurst Clinic, 2901 Washington St., Vicksburg, MS 39180 **Clorazepate dipotassium, diazepam and placebo in chronic anxiety.** Current Therapeutic Research. 15(7):449-459, 1973.

The effects of clorazepate dipotassium (CD), a new benzodiazepine, diazepam (DP) and a placebo were tested in a double-blind trial in chronic, moderately severe anxiety with 63 Ss and 27 controls. CD induced an excellent overall therapeutic response in 25 of 32 Ss as compared with two of 31 on DP and one of 27 on placebo. Reductions of rating scale scores for anxiety were greater in patients on CD than in patients on DP or placebo. Side effects were reported by 59% of

Ss on CD, 58% on DP and 11% on placebo. No adverse effects were revealed by physical, ophthalmoscopic or clinical laboratory examinations done before and after the 28 day trial. 4 references. (Journal abstract modified)

167345 Falk, Marshall A. 4700 N. Clarendon Ave., Chicago, IL 60640 **The computer analyzes two psychotherapeutic agents in anxiety/depressed states.** Current Therapeutic Research. 15(7):488-499, 1973.

Use of a computer to analyse two psychotherapeutic agents in anxiety - depressed states is reported. A statistically reliable psychotic index scale was used in analysing effects of perphenazine/amitriptyline (P/A) and chlorpromazine over a 5 week period. The index of 16 anxiety - depression variables was completed for the pretreatment visit and at 5 weekly followup visits. A statistical evaluation of the data was carried out utilizing the analysis of covariance approach. Statistically, both drugs demonstrated similar effectiveness in almost all 16 variables. P/A proved statistically superior in four areas: mood, anxiety, delusions and insight, in its clinically recommended area of anxiety and depression. At the end of the test, improvement on four other variables was noted. Also, the general appearance, manner and thought content of the patients improved. 3 references. (Journal abstract modified)

167346 Nanivadekar, A. S.; Wig, N. N.; Khorana, A. B.; Master, Roshen S.; Kulkarni, S. S. Wyeth Laboratories Ltd., Bombay, India **A multicenter investigation of lorazepam in anxiety neurosis.** Current Therapeutic Research. 15(7):500-507, 1973.

Employing a standardized protocol, a multicenter investigation was carried out to compare lorazepam (LP) and diazepam (DP) in anxiety neurosis with 98 patients. In the first 2 weeks of the 4 week trial, LP brought about a significantly greater fall in Hamilton scale score than DP; there was also a consistent trend in favor of LP with respect to global improvement. After 4 weeks there was no significant difference by either criterion. Incidence of sedative side-effects was significantly less on LP. 5 references. (Journal abstract modified)

167575 Johnson, F.; Sacco, F. A.; Yellowley, T. W. Ryton-on-Tyne, Durham, England **Chlordiazepoxide and dothiepin compared in anxiety/depression in general practice.** Practitioner. 211(1263):362-364, 1973.

A study in which 87 patients with tension, anxiety and emotional disturbances, including depression, took part in a 3 week, double-blind trial of chlordiazepoxide and dothiepin is discussed. Results indicate that dothiepin is significantly better in overall relief symptoms than chlordiazepoxide. Findings illustrate that drowsiness occurred less often with dothiepin than with chlordiazepoxide, but that other side-effects were equal in incidence. 3 references. (Author abstract modified)

167594 Grattarola, F. R.; Morgando, E. Division Neurologica, Ospedale S. Giovanni, 10100 Torino, Italy **/Clinical experimentation with a new benzodiazepine in the management of phobic and obsessive symptoms./** Sperimentazione clinica di un nuovo derivato della serie benzodiazepinica: il bromazepam (Ro 5-3350), nel trattamento dei sintomi fobico-ossessivi. Minerva Medica (Torino). 64(40):2107-2111, 1973.

Results of clinical experiments using bromazepam (Ro 5-3350), a new benzodiazepam, in 39 cases of psychoneurosis with predominantly phobic obsessive symptoms are tabulated and discussed. A double-blind pilot study involved 20 cases, and satisfactory therapeutic results were obtained. Resolution of neurotic anxiety was more effective than had been anticipated, particularly in cases where phobia and obsession were present. 4 references.

167773 Rickels, Karl; Pereira-Ogan, Jorge A.; Chung, Hack R.; Gordon, Paul E.; Landis, William B. 203 Piersol Bldg., University Hospital, 3600 Spruce St., Philadelphia, PA 19104 **Bromazepam and phenobarbital in anxiety: a controlled study.** Current Therapeutic Research. 15(10):679-690, 1973.

The efficacy of bromazepam as an antianxiety agent in relation to phenobarbital and placebo was assessed with three neurotic outpatient populations. The 4 week double-blind trial with 115 Ss showed that bromazepam and phenobarbital produced significantly more improvement than placebo only in the moderately ill but not in the mildly ill anxious neurotic outpatient. Low socioeconomic class clinic Ss responded particularly poorly to bromazepam and phenobarbital. Secondarily depressed anxious Ss improved more with both compounds than Ss without such secon-

dary features. Bromazepam produced significantly more sedative side-effects than either phenobarbital or placebo. Suggestions are offered for the design of further studies in order to determine the appropriate role of bromazepam in neurotic anxiety. 15 references. (Author abstract modified)

168316 Kellner, Robert. Department of Psychiatry, University of New Mexico, Albuquerque, NM **Chlordiazepoxide in depressive neurosis: an open label cross-over study with amitriptyline.** Canadian Psychiatric Association Journal (Ottawa). 18(5):393-398, 1973.

Sixty five depressed outpatients were treated in an open label cross-over study of chlordiazepoxide and amitriptyline. The treatment was changed only in those patients in whom the response to the first medication was inadequate. Global rating and self-rating scales were compounded into a rating of treatment preference. For the group as a whole, chlordiazepoxide appeared to be more effective than amitriptyline. Chlordiazepoxide appeared to be more effective in patients who were initially diagnosed as suffering from exogenous depressions, whereas amitriptyline appeared to be more effective in those with endogenous depressions. The findings suggest that in a large proportion of depressed patients, it is possible to predict from thier clinical features which class of psychotropic drugs is likely to be more effective. 14 references. (Author abstract modified)

168832 Tyrer, Peter; Candy, Julian; Kelly, Desmond. Dept. of Psychiatry, Univ. of Southampton, Southampton, England **A study of the clinical effects of phenelzine and placebo in the treatment of phobic anxiety.** Psychopharmacologia (Berlin). 32(3):237-254, 1973.

The results of a double-blind controlled trial of phenelzine and placebo in chronic agoraphobic and socially phobic psychiatric outpatients were reported. During the 8 weeks of treatment, 32 Ss were given flexible doses of phenelzine or placebo. Ss were prospectively matched in pairs so that clinical response could be assessed in detail. Phenelzine was significantly superior to placebo on a number of measures particularly for overall assessment. The treatment differences were not significant after 4 weeks treatment but were so at 8 weeks. The correlates of response and the results of the clinical ratings suggest that phenelzine is not acting as an antidepressant in this population. 62 references. (Author abstract modified)

169089 Covi, Lino; Lipman, Ronald S.; Derogatis, Leonard R. Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD **Imipramine, diazepam and group psychotherapy in long-term treatment of depressive neurotics.** Psychopharmacology Bulletin. 9(4):57-59, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, a six cell (imipramine, diazepam, or placebo with group psychotherapy or minimal supportive group therapy contact) study of the long-term treatment of depressive neurotics was evaluated. A preliminary analysis of the outcome measures in the areas of symptomatology and mood as well as global measures of improvement were accomplished on a sample of 94 patients. With all measures, imipramine was found to be superior to both diazepam and placebo. There was a consistent lack of main effects associated with the type of therapy throughout the symptom and mood measures. Global ratings by patient, by doctor, and by significant relative or friend showed similar drug effects and a lack of type of therapy effects. 1 reference. (Journal abstract modified)

169286 Still, Charles N.; Ham, Charles H., Jr. no address **Vesta variant of Tourette's disease: treatment with haloperidol.** Southern Medical Journal. 66(11):1222-1225, 1973.

A case study of an adult variant of the classic maladie des tics was made to determine the effects of haloperidol on the tics. Haloperidol derives its neuroleptic effects by blocking dopamine receptors of the central nervous system. Recurrence of tics four days after stopping haloperidol, then prompt control by resuming the drug indicates a degree of effectiveness in controlling tics. Development of parkinsonian side-effects suggests overcorrection toward central cholinergic dominance. 15 references.

169632 Gilbert, Michael M.; Koepke, Hans H. Dept. of Psychiatry, University of Miami Medical School, Coral Gables, FL 33124 **Relief of musculoskeletal and associated psychopathological symptoms with meprobamate and aspirin: a controlled study.** Current Therapeutic Research. 15(11):820-832, 1973.

A double-blind clinically controlled trial of aspirin and meprobamate was conducted to compare the results with those of placebo in the treat-

ment of patients suffering from moderate to severe musculoskeletal symptoms associated with anxiety. Patients suffering from pain, cramps, and spasm associated with anxiety were chosen as subjects from a population of outpatients in a neuropsychiatric practice in Florida. All data were analyzed by factorial analysis, testing for main drug effects and drug interaction. It was found that aspirin reduced pain but did not affect emotional symptoms, and that meprobamate was significantly effective against emotional stress, but reduced pain to a lesser degree. The combination of these two drugs was best: it appears that the effects of both drugs were additive without any interaction. Side-effects are also discussed in detail. 9 references. (Journal abstract modified)

171124 Weiss, A. A.; Robinson, S.; Dasberg, H. Talbieh Psychiatric Hospital, P.O. Box 39, Jerusalem, Israel **Changes in mental functioning accompanying anti-psychotic drug therapy.** Israel Annals of Psychiatry and Related Disciplines (Jerusalem). 11(2):134-140, 1973.

Changes in mental functioning accompanying antipsychotic drug therapy is discussed. Ten patients on antipsychotic drug treatment were administered a color form sorting test, and a visual retention test before and after initial examination. Significant improvement from initial to second followup examination was observed. This improvement is discussed in terms of improvement and emergence from a regressive state beyond the confines of classical neurosis to a more mature level of ego functioning. 14 references. (Author abstract modified)

171162 Setyonegoro, R. K. no address **The problem of anxiety in a non-western society: a combined chemo and psychotherapeutic approach.** Indonesian Psychiatric Quarterly (Djakarta). 5(4):92-98, 1972.

A combined chemotherapeutic and psychotherapeutic approach toward anxiety among people in nonwestern society is reported. Phase I is the chemotherapeutic stage in which the patient is given only drugs. Phase II introduces psychotherapeutic methods and reinforces ego functioning to manage anxiety. Phase III emphasizes the difference between chemotherapy alone and combined chemo and psychotherapy. It also concludes the therapeutic sessions with some insight on the part of the social and cultural determinants of behavior which is in many cases westernization. The role of the priest and the nobility are also discussed.

171924 Klerman, Gerald L.; Dimascio, Alberto; Weissman, Myrna; Prusoff, Brigitte; Paykel; Eugene S. Department of Psychiatry, Harvard Medical School, Boston, MA **Treatment of depression by drugs and psychotherapy.** American Journal of Psychiatry. 131(2):186-191, 1974.

The efficacy of the tricyclic antidepressant amitriptyline and psychotherapy, alone and in combination, in preventing the relapse of 150 neurotic depressed female patients was tested. Patients receiving amitriptyline and little psychotherapy had a 12% relapse rate, compared to a 16% rate for those receiving more psychotherapy and no medication. There was significant difference between drug therapy alone or drug therapy in combination with psychotherapy. Psychotherapy was beneficial to patients with problems of social adjustment and interpersonal relations. 22 references. (Author abstract modified)

171925 Covi, Lino; Lipman, Ronald S.; Derogatis, Leonard R.; Smith, James E., III.; Pattison, Joseph H. Johns Hopkins School of Medicine, Baltimore, MD 21205 **Drugs and group psychotherapy in neurotic depression.** American Journal of Psychiatry. 131(2):191-198, 1974.

Drugs and psychotherapy were examined in the treatment of depression. Chronically depressed neurotic women outpatients were randomly assigned, after a 2 week placebo washout period, to receive one of three medications (imipramine, diazepam, or placebo) and to either weekly group psychotherapy or biweekly brief supportive sessions at one of two clinics. Analyses of covariance for the first 16 weeks of active treatment indicated a marked therapeutic advantage for imipramine on most of the outcome measures. No advantage for group therapy was detected on these measures. Patients who showed improvement were continued in further controlled drug treatment for up to a total of 71 weeks; preliminary analyses of this phase showed some continuing advantage for treatment with imipramine. 16 references. (Author abstract)

172485 Sakalis, G.; Pearson, E.; Kermani, E.; Gershon, S. Neuropsychopharmacology Research Unit, New York University Medical Center, 550 First Ave., New York, NY **On the anti-anxiety properties of a new benzodiazepine, ORF 8063.** Current Therapeutic Research. 15(5):268-271, 1973.

The antianxiety activity of the benzodiazepine compound ORF 8063 is examined. The study corroborates previous findings which suggest that ORF 8063 produces antianxiety activity in some patients. Despite the observation that medication had to be administered in two to three divided doses, rather than a single one, ORF 8063 merits further investigation in regard to the relationships between positive clinical activity and blood levels. 4 references. (Journal abstract modified)

172486 Rosenthal, Saul H.; Bowden, Charles L. Department of Psychiatry, University of Texas Medical School, San Antonio, TX **A double-blind comparison of thioridazine (Mellaril) versus diazepam (Valium) in patients with chronic mixed anxiety and depressive symptoms.** Current Therapeutic Research. 15(5):261-267, 1973.

A group of semichronic outpatients with mixed neurotic symptoms of anxiety and depression were treated on a double-blind basis with adjustable doses of diazepam and thioridazine. Both groups showed significant improvement on individual symptom ratings, Sum Hamilton ratings, and on global ratings. Thioridazine was significantly superior to diazepam in a group of symptoms representing depressive symptomatology including suicide, psychomotor retardation, helplessness, worthlessness, and guilt feelings. Diazepam was significantly superior to thioridazine on anxiety symptoms including somatic anxiety, psychic anxiety, and early insomnia. Thioridazine showed slightly greater improvement on global ratings of change in rating of illness, rating of improvement, and on Sum Hamilton scores. 4 references. (Journal abstract modified)

172993 Rickels, Karl; Csanalosi, Irma; Chung, Hack R.; Case, W. George; Pereira-Ogan, Jorge A.; Downing, Robert W. Psychopharmacology Research Unit, Philadelphia General Hospital, Philadelphia, PA 19104 **Amitriptyline in anxious-depressed outpatients: a controlled study.** American Journal of Psychiatry. 131(1):25-30, 1974.

In a 4 week study of 108 volunteer subjects with mixed symptoms of anxiety and depression, amitriptyline produced significantly more improvement than placebo. Significant differences were noted between the amitriptyline and placebo treatment groups at 2 weeks in relief of somatic and anxiety symptoms and at 4 weeks in relief of depressive symptoms. The marked sensitivity of the volunteers to certain amitriptyline induced side-effects appeared to be related to their relatively high level of education, employment, and anxiety. Comparison data indicated that the results obtained with volunteers are relevant to outpatients treated in general practice. 14 references. (Author abstract)

174495 Ostow, Mortimer. 5021 Iselin Avenue, Riverdale, The Bronx, NY 10471 **Rapid and gentle pharmacotherapy of depression.** New York State Journal of Medicine. 74(1):74-77, 1974.

The usefulness and limitations of drugs used to treat depression are discussed. The primary antidepression chemicals, that is, the tricyclic and monomine oxidase psychic energizers, can be replaced in some instances, or supplemented in others, by more rapid or less distressing agents or procedures. These less disturbing agents also increase the proportion of patients who can be helped by pharmaceutic therapy. These include small doses of lithuim carbonate, small doses of thiothixene, and deanol. Intramuscular administration of the tricyclic compounds can reduce the latency between the beginning of therapy and relief from depression. Six case studies are presented to show various applications of lithium carbonate, thiothixene and deanol separately or supplementary to tricyclic and monoamine oxidase inhibitors. (Author abstract modified)

174777 Ekiert, Halina; Gogol, Zofia; Welbel, Leszek; Buchowska, Irena. Instytut Psychoneurologiczny w Pruszkowie, ul. Partyzantow 2/4, Poland **/Electroclinical aspect of insidon treatment in patients with neurotic symptoms./** Elektrokliniczny aspekt leczenia insidonem chorych z objawami nerwicowymi. Psychiatria Polska (Warszawa). 7(2):169-177, 1973.

Results of treating 37 patients, 24 men 13 women, with neurotic symptoms and normal or abnormal EEG tracings with maximum oral doses of 150 to 200 mg Insidon for over 6 weeks are detailed. The effect of the drug on 13 neurotic symptoms was studied, as were the EEG tracings. Examinations were conducted prior to treatment and 2, 4, and 6 weeks after completion of treatment. The therapeutic effects (the number and kind of improvements in the clinical state, and the behavior of the different neurotic symptoms) are as described in the literature. Modifications in the EEG tracings of 24 patients did not correlate with clinical improvement. The incidence of changed tracings was greater in patients with lesion to the central nervous system than in those free of these

lesions. It is concluded that Insidon, a drug in the thymoleptics group, is comparable to Imipramine in its therapeutic action and influence on the EEG tracing, but should be used with caution in patients with marked lesions to the central nervous system and abnormal EEG tracings. 22 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

167335 Defelice, Eugene A.; Chaykin, Louis B.; Cohen, Albert. Scientific Affairs and Commercial Development, Sandoz-Wander, Inc., Hanover, NJ 07936 **Double-blind clinical evaluation of mazindol, dextroamphetamine, and placebo in treatment of exogenous obesity.** Current Therapeutic Research. 15(7):358-366, 1973.

Mazindol, dextroamphetamine and placebo were studied as anorexigenic agents in 90 exogenously obese outpatients during 6 weeks of therapy. Results show that Mazindol produced a greater amount of total weight loss than did dextroamphetamine or placebo. Mean weight losses for the three compounds are included. Side effects were mild, with sporadic complaints of central nervous stimulation, nervousness, dizziness, dry mouth, nausea, constipation and slightly elevated standing pulse, but dropouts were few. No physical or psychological dependence was found. 20 references. (Author abstract modified)

167338 Crawford, Thomas I. Dept. of Anesthesiology, Maricopa County General Hospital, Phoenix, AZ **Preanesthetic medication in elective surgery: comparison of intravenous diazepam with meperidine.** Current Therapeutic Research. 15(7):441-448, 1973.

Diazepam (DP) and meperidine (MP) are compared as preanesthetic medication. A double-blind study to determine whether DP or injectible Valium, substituted for MP could produce adequate sedation in patients scheduled for major elective surgery with inhalation anesthesia is reported. Results indicate that DP is an effective, safe preanesthetic medication for reducing preoperative anxiety as well as postsurgical excitement and restlessness. The drug produced minimal effects on cardiorespiratory indices and the amnesic effects of DP were significantly greater with DP than with MP. 15 references. (Journal abstract modified)

167340 Tosi, G. C.; Tosi, E. C.; Hattab, J. R. Divisione di Chirurgia Generale, Ospedale Generale di Zona, S. Maria e S. Caterina, CEVA (Cn) Italy **The use of N-demethyldiazepam in outpatients suffering from insomnia.** Current Therapeutic Research. 15(7):460-464, 1973.

Use of N-demethyldiazepam (N-d) in outpatients suffering from insomnia is reported. Patients had previously been treated with nitrazepam. N-d was effective for the induction and maintenance of sleep in 22 male and female Ss suffering from insomnia. Awakening was normal and without hangover. The dosage prescribed gave a valid and positive response without undesirable side-effects. 15 references. (Journal abstract modified)

167496 Banen, David M.; Resnick, Oscar. Cushing Hospital, Framingham, MA 10701 **Lorazepam versus glutethimide as a sleep-inducing agent for the geriatric patient.** Journal of the American Geriatrics Society. 21(11):507-511, 1973.

The safety of lorazepam was compared with that of glutethimide in 50 chronically ill geriatric patients. Repeated physical examinations, laboratory determinations and other tests indicated that any organic disease in these patients was stabilized before the study and was not affected by the test drugs. Early morning drowsiness, dizziness and lethargy were noted with each drug during the first 2 weeks. More patients in the glutethimide series discontinued therapy because of side-effects than in the lorazepam series. Dosage reduction to 1mg nightly was necessary in many of those treated with lorazepam. Results indicated that lorzepam is useful for aiding elderly patients to sleep. An initial dosage of 1mg nightly can usually be increased to 2mg nightly with safety. 6 references. (Author abstract modified)

168314 Frost, J. B. Central Newfoundland Hospital, Grand Falls, Newfoundland, Canada **Mesoridazine and chlorpromazine in the treatment of alcohol withdrawal syndrome.** Canadian Psychiatric Association Journal (Ottawa). 18(5):385-387, 1973.

Forty patients admitted for the treatment of alcohol withdrawal were placed on either chlorpromazine or mesoridazine on a double-blind basis. No significant difference in rate or degree of improvement between the two groups was noted and both groups showed an improvement which was more marked in the first week of treat-

ment. There were few significant side-effects from either drug. Improvement on either therapeutic regime is predictable and both are effective in relieving or lessening agitation, tremulousness, hallucinations, and anxiety in patients recovering from acute acohol intoxication. 8 references (Author abstract)

168315 Lacny, J. Saskatchewan Training School, Moose Jaw, Saskatchewan, Canada **Mesoridazine in the care of disturbed mentally retarded patients.** Canadian Psychiatric Association Journal (Ottawa). 18(5):389-391, 1973.

The effectiveness of mesoridazine in comparison with other previously used psychotropic drugs in the control of behavioral problems of mental retardation was studied. Forty five mental retardates were chosen at random for a 9 month study. A significant improvement occurred in all but two of the sixteen items evaluated. Improvement was greater in those symptoms related to poor control of impulse, belligerence and motor excitement. Side-effects consisted mainly of drowsiness, pallor, dry mouth, tremors, and unsteadiness. There was no increase in the incidence of epileptic seizures and no abnormal laboratory findings were observed. Mesoridazine appears to be an effective psychotropic drug in the control of some aspects of disturbed behavior in severely retarded patients. 6 references.

168369 Vignalou, J.; Beck, H. Hopital-Hospice d'Ivry, 7, avenue de la Republique, F-94203 Ivry-sur-Seine, France **/L-dopa in 122 cases of Parkinson's disease at age 70 or over. A comparative study with a group of patients aged 41 to 69 years./** La L-dopa chez 122 Parkinsoniens de plus de 70 ans. Etude comparative avec un groupe de parkinsoniens ages de 41 a 69 ans. Gerontologia Clinica (Basel). 15(1):50-64, 1973.

A study of the therapeutic effects of L-dopa in Parkinson's syndrome in 122 patients aged 70 to 90 years is reported, and a comparison is made with a control group of 153 cases, aged 41 to 69 years. The therapeutic experience extended over a period of 1 year. Overall results of both groups are not statistically different. The observed efficacy of L-dopa on symptoms such as akinesia, trembling and hypertonia was directly proportional to the severity of the symptoms prior to treatment. This efficacy was the same for the three symptoms, for the same initial severity and for the same period of 1 year. The effect on walking and functional activities is parallel with that on the Parkinsonian symptoms. The apparent frequency of intolerance accumulated over a year of treatment totals 83% of the cases. On the whole, results of the treatment of Parkinson's syndrome with L-dopa are as favorable in patients above age 70 as in those below. (Author abstract modified)

168803 Udabe, R. Ucha. Dept. of Psychiatry, Univ. of Buenos Aires, Buenos Aires, Argentina **Clinical experience with a new psychotropic drug, trazodone: a review of literature.** Current Therapeutic Research. 15(10S):755-763, 1973.

A literature review of the clinical investigation of trazodone is presented. A marked antidepressive action of the drug has been established. The type of depression which responds most favorably has not been defined. Since a considerable tranquilizing activity has been established, trazodone has been found useful in the treatment of anxiety states as well as in preanesthesia and in the preparation of patients for uncomfortable procedures. Tolerance of the drug is good and only slight and transient side-effects have been encountered in a few patients. Trazodone is a potent, well-tolerated psychotropic drug endowed with antidepressant and tranquilizing action and is therapeutically active in a number of different conditions. 35 references. (Author abstract modified)

168805 Nair, N. P. V.; Ban, T. A.; Hontela, S.; Clarke R. Clinical Investigational Unit (Douglas Hospital), Div. of Psychopharmacology, Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **Trazodone in the treatment of organic brain syndromes, with special reference to psychogeriatrics.** Current Therapeutic Research. 15(10S):769-775, 1973.

A geriatric study of trazodone was made. In an uncontrolled clinical study, trazodone was administered for 12 weeks to 10 elderly patients with organic brain syndrome. There was a statistically significant improvement in the parameters of organicity, arousal, integration and mood. Maximal improvement was seen on a dose of 100mg/day. It was speculated that the improvement in organicity was related to facilitation of restoration of the balance between arousal and integration which has been claimed to be impaired in organic brain syndrome patients. 8 references. (Author abstract modified)

168806 Galvan, L.; Nair, N.P.V.; Kussin, D.; Ban, T. A. Clinical Drug Evaluation Unit (Douglas Hospital), Div. of Psychopharmacology, Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **Trazodone in the treatment of schizophrenias.** Current Therapeutic Research. 15(10S):776-780, 1973.

The use of the phenyl-piperazine derivative or triazolo-pyridine, trazodone, in the treatment of schizophrenias was reported. In a 12 week uncontrolled clinical trial with trazodone in chronic hospitalized Ss, no significant antipsychotic effect of the drug could be revealed. It was noted that optimal therapeutic effects were present in the dosage of 300mg/day and that higher dosages may have had a negaive therapeutic effect. Since drug withdrawal resulted in enchancement of deterioration, the possibility was raised that trazodone may have antipsychotic properties in a different dosage range. The drug may also have antidepressant properties which need to be explored. 2 references. (Author abstract modified)

168807 Amin, M.; Ban, T. A.; Klingner, A. Early Clinical Drug Evaluation Unit, Div. of Psychopharmacology, Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **Trazodone in the treatment of affective disorders.** Current Therapeutic Research. 15(10S):781-788, 1973.

An uncontrolled single-blind clinical trial with trazodone, a new trianzolo-pyridine preparation, was carried out with 10 depressed psychiatric patients. Findings suggest that trazodone has therapeutic action in depressed Ss when given in the dosage of 75mg/day. The possibility was raised that, of the various depressions, serotonergic depression is the one which responds favorably to trazodone administration. 6 references. (Author abstract)

168808 Knobel, M. Dept. of Psychiatry, School of Medicine, Univ. of Buenos Aires, Buenos Aires, Argentina **Trazodone and psychosomatic medicine.** Current Therapeutic Research. 15(10S):789-798, 1973.

The use of trazodone in psychosomatic medicine was reported. A double-blind study of 100 adult Ss with different common somatic disturbances was made with the addition of trazodone to their usual treatment. The drug was useful in shortening treatments and improving mood and social capacity in a statistically significant ratio. The presence of depression was detected. The effective psychotropic action of trazodone, which clearly differentiated the Ss receiving it from those receiving placebo or another anxiolytic agent, seems to prove the presence of a depressive nucleus in what can be called psychosomatic disorders. It was postulated that an antidepressant anxiolytic drug such as trazodone would be useful in such cases. No side-effects and no interference with the specific mediation used in each disease were noted. 22 references. (Author abstract modified)

168809 Antonelli, F.; De Gregorio, M.; Dionisio, A. Research Dept., Italian Society of Psychosomatic Medicine, Rome, Italy **Trazodone in the treatment of psychoneuroses: a double-blind study.** Current Therapeutic Research. 15(10S):799-804, 1973.

A clinical investigation in the area of psychoneurosis was made to examine the therapeutic range of trazodone. Ss were 30 psychoneurotic outpatients who were treated and evaluated for the following symptomatologic cluster: typical manifestations; somatization and psychosomatic reactions; disorders of sleep pattern; disorders of ideation; psychomotor disorders; and behavioral disorders. Results indicated that a reduction of at least 50% in the clinical symptomatology was observed in 10 out of 15 Ss treated with trazodone and in three out of 15 Ss treated with placebo. A 75mg dosage of trazodone seems to be a therapeutically effective agent in the treatemnt of psychoneurotic patients and its effect is detectible as early as the seventh day of treatment. 24 references. (Author abstract modified)

168923 Boueri-Atem, Salomon; Brahim, D.; Curi, O. Department of Infectious Diseases, University of Cuyo, Mendoza, Argentina **Oxazepam in allergic conditions.** Clinical Medicine. 80(10):11-13, 1973.

The effect of oxazepam was investigated in 49 allergic patients who exhibited a significant emotional component to their illness. Oxazepam was given in a dosage of 15mg three times a day for adults, 15mg twice a day for older children, or 7.5mg twice a day for children under 2 years. Other medications were administered as required. Complete remission of all symptoms (including asthma, skin lesions, bronchitis, rhinitis, and conjunctivitis) was obtained in 24 patients, and a satisfactory response (both allergic and emotional) was obtained in 36. Results indicate that ox-

azepam is useful for relieving anxiety and other nervous symptoms which accompany an allergy and make usual antiallergic measures ineffective. 19 references. (Author abstract modified)

169065 Prien, Robert F. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD **Chemotherapy in chronic organic brain syndrome - a review of the literature.** Psychopharmacology Bulletin. 9(4):5-20, 1973.

A review of the chemotherapy literature in chronic organic brain syndrome (diffuse impairment of brain tissue function) is presented with emphasis on restrictions on pharmacological treatment caused by physical illnesses in the patient. The psychotropic drugs covered are: antipsychotic, antianxiety, sedative hypnotic, and antidepressants. The drugs influencing cerebral circulation are: cerebral vasodilators, ergot alkaloids (hydergine), and anticoagulants. The central nervous system stimulants of pipradrol (Meratran, methylphenidate (Ritalin), deanol (Deaner), the amphetamines, pentylenetetrazol (Metrazol), ethamivan (Emivan), and caffeine are covered. Pure oxygen therapy is also discussed. 184 references.

169138 Watts, Geoff. New Medical Journals, Ltd., Clareville House, 26-27 Oxendon St., London SW1Y 4EL, England **Changing death's perspective.** World Medicine (London). 9(2):15-19, 1973.

The use of lysergic acid diethylamide (LSD) with dying patients is reported. Patients in the treatment program are selected as follows: having a terminal illness; be suffering emotional discomfort, physical pain, anxiety, tension of fear of death; the patient and the family must give informed consent; and the patient must have a survival expectancy of at least three months. The treatment falls into three phases -- preparation, the LSD session and subsequent drug free interviews. Results of the session reveal that patients are less anxious, depressed, socially withdrawn and do not suffer from insomnia. Value systems also change. The future of the treatment is discussed.

169152 Ghate, Vijay R. Dorothea Dix Hospital, South Boylan Ave., Raleigh, NC 27611 **Antipsychotic agents.** North Carolina Medical Journal. 34(11):859-865, 1973.

Concise information on the use of antipsychotic agents is presented. Drugs are the most important tool in the hands of the psychiatrists, but certain limitations must be considered, and the types of disorders for which drug therapy is indicated in conjunction with other measures must be delineated, along with primary aims of management. Antipsychotic drugs are primarily divided into three classes: phenothiazines, thioxanthenes, and butyrophenones, each of which has distinct pharmacological properties and specific side-effects and toxicities. It is important to choose the proper drug, considering such factors as susceptibility, age, pregnancy, history of mental illness, and symptomatology. One compound which does not fall into the category of other tranquilizers is lithium carbonate, in widespread use in manic-depressive psychosis. Finally, drug therapy in children with psychiatric or emotional disorders has proven useful when used as adjuncts to other forms of therapy. 16 references.

169220 Miller, Edith; Nieburg, Herbert A. Department of Medicine, Division of Neurology, Maimonides Medical Center, New York, NY **Amphetamines: valuable adjunct in treatment of Parkinsonism.** New York State Journal of Medicine. 73(22):2657-2661, 1973.

The value of amphetamine therapy as an adjunct in treating Parkinson's disease was investigated, stressing the effectiveness of drugs in increasing motivation for improvement. All patients had been treated with levodopa over a 3 year period, with 45 out of 204 showing limited success due to lack of motivation, mainly due to advanced age, severe depression, and being bedridden. Fifteen of the 45 Ss showed contraindication to the drugs and were used as controls, while 30 patients received dextroamphetamine sulfate or methylphenidate hydrochloride in a maximal dosage of 10mg per day. In the treated group, the improvement score was raised by a mean of 31%, whereas the controls failed to make any improvement. An additional 21 patients received methylphenidate hydrochloride for levodopa induced lethargy and somnolence. In all instances, these side-effects were abolished. Laboratory abnormalities or cardiovascular side-effects were not observed. 7 references.

169295 Gross, Mortimer D. 1893 Sheridan Road, Highland Park, IL 60035 **Imipramine in the treatment of minimal brain dysfunction in children.** Psychosomatics. 14(5):283-285, 1973.

A report on imipramine as an effective drug in the treatment of minimal brain dysfunction (MBD) in children where methylphenidate (Ritalin) and dextroamphetamine are ineffective is presented. Imipramine is sometimes useful as a supplement to methylphenidate and dextroamphetamine, particularly when the symptom of enuresis is present (the imipramine is given at bedtime). Its toxicity appears to be quite low; a few major side reactions quickly disappeared when the medication was stopped. It is suggested that imipramine should be considered in all cases of MBD when neither dextroamphetamine nor methylphenidate prove effective. 4 references.

169298 Krakowski, Adam J.; Engisch, Robert. Div. of Psychiatric Research, Champlain Valley-Physicians Hospital Medical Center, Plattsburgh, NY **A new agent for chemotherapy of migraine headaches: a controlled study.** Psychosomatics. 14(5):302-308, 1973.

A study of the chemotherapeutic value of the drug BC-105 in a group of ambulatory patients diagnosed as having either classic or common migraine headache is presented. The study evaluated the efficacy and safety of the drug as a migraine prophylactic and its efficacy upon the mood of the treated patient. The overall impression was that BC-105 is an effective drug which compares favorably with other drugs in the interval treatment of migraine headaches. Its usefulness is enhanced by its safety, absence of toxicity, and an apparent antidepressant quality. It is suggested that these factors make BC-105 useful in those cases which require prolonged interval treatment. 5 references.

169461 Nagaswami, S.; Nagaswami, R. Neurology Service, 2200 Gage Blvd., Veterans Administration Hospital, Topeka, KS 66622 **Amantadine hydrochloride in treatment of parkinsonism.** Diseases of the Nervous System. 34(5):253-258, 1973.

Amantadine hydrochloride is examined as an antiparkinsonian medication for mild to moderate parkinsonism, hemiparkinsonism and drug induced parkinsonism. It is safe to administer in patients with hepatic, renal and cardiac disease, glaucoma and peptic ulcer. Preexisting or associated with parkinsonism psychiatric disorders were not aggravated. The drug proved generally more efficacious than anticholinergic drugs, and tended to potentiate their cholinergic side reactions. It was not found useful to combine amantadine with anticholinergic drugs. The drug was of limited to no benefit in postencephalitic parkinsonism. L-dopa proved a more potent antiparkinsonian drug for postencephalitic parkinsonism and for moderate to severe bilateral parkinsonism. Its usefulness was limited by the aggravation of a number of preexisting or associated diseases, and the universal incidence of side-effects, some of which preclude optimum therapeutic dosage levels. Combinations of L-dopa and amantadine were useful in patients who could not tolerate a high level intake of L-dopa. No permanent adverse reactions were found in patients who had been on amantadine therapy up to 40 months. 16 references. (Author abstract modified)

169633 Kawathekar, Pushpa; Anusuya, S. R.; Sriniwas, Pushpa; Lagali, S. Dept. of Obstetrics and Gynecology, M. R. Medical College, Gulbarga (585105), India **Diazepam (Calmpose) in eclampsia: a preliminary report of 16 cases.** Current Therapeutic Research. 15(11):845-855, 1973.

The use of diazepam in eclampsia cases in an obstetric unit in India during the last two years is reported. Sixteen cases of eclampsia were treated with Calmpose administered parenterally before and 24 hours after delivery and thereafter orally for another week. Control of convulsions was achieved completely within 30 minutes in 13 of the cases and in all cases within 4 hours. Recurrence was observed once. There was only one maternal death. Absence of maternal complications like cardiac, renal and respiratory failures was a noteworthy feature with diazepam therapy. The foetal outlook is considered to be better as 11 of the 12 babies that were born alive did not require resuscitation and were active at birth. No side-effects of the drug therapy were observed. Diazepam was found to be safe, simple, and effective in the management of eclampsia. 27 references. (Journal abstract modified)

169634 Grabowski, Stanislaw W. Ellisville State School, Ellisville, MS 39437 **Safety and effectiveness of haloperidol for mentally retarded behaviorally disordered and hyperkinetic patients.** Current Therapeutic Research. 15(11):856-861, 1973.

The use of haloperidol in controlling disruptive motor, emotional, and behavioral symptoms in mentally retarded students at a state school in Mississippi is reported. Almost 150 students were transferred from phenothiazines to haloperidol and prophylactic benztropine mesylate. It was

discovered that hyperkinesis was reduced and marked improvement was achieved in social behavior, attention and concentration, integrative skills, behavior, and emotion. No improvement, however, was achieved in speech or communications. Clincial laboratory values remained within normal limits. It is concluded that haloperidol appears to be the safest and most effective chemotherapeutic agent presently available for the treatment of emotionally disturbed and/or hyperkinetic mentally retarded patients. Two case studies are also included. Further medical investigations in the special education field are recommended. 5 references. (Journal abstract modified)

169746 Dufficy, Rafael G., Jr. Department of Professional Education, Napa State Hospital, Imola, CA 94558 **Use of psychotherapeutic drugs in the acute detoxification of heroin addicts.** Military Medicine. 138(11):748-751, 1973.

A group of 1000 heroin addicts, all of them voluntary admissions to a state hospital, participated in a study to determine whether total detoxification, with alleviation of both physical and psychological symptoms, could be achieved with methadone and a minimum of supportive drug therapy. Two individual programs of management are described and results compared. The second program included use of the psychotropic drug, doxepin. While methadone does detoxify the addict physically, it apparently does not affect his psychological dependency. With use of doxepin, patients appeared to gain some degree of emotional stability, which increased their ability to resist the psychic craving for heroin. 10 references. (Author abstract)

169861 Buchsbaum, Monte; Wender, Paul. National Institute of Mental Health, Bldg. 10, Room 2N-315, Bethesda, MD 20014 **Average evoked responses in normal and minimally brain dysfunctioned children treated with amphetamine: a preliminary report.** Archives of General Psychiatry. 29(6):764-770, 1973.

Visual and auditory average evoked responses (AERs) were studied in 24 minimally brain dysfunctioned (MBD) children and 24 age and sex matched normal controls. MBD children showed AERs characteristic of relatively younger normal children. MBD children who showed clinical improvement on amphetamine tended to show these immature patterns of AER response off drug to a greater extent than MBD amphetamine nonresponders. Pretreatment AER was successfully used to predict drug response; responders could be separated from normal children with 64% accuracy. Amphetamine related AER changes were also in opposite directions in responder and nonresponder MBD children. The data support the concept of a neurophysiological maturational lag in MBD children. 25 references. (Journal abstract)

170129 Kirven, L. E.; Montero, E. F. Central State Hospital, Petersburg, VA **Comparison of thioridazine and diazepam in the control of nonpsychotic symptoms associated with senility: double-blind study.** Journal of the American Geriatrics Society. 21(12):546-551, 1973.

The effects of thioridazine and diazepam were studied by the double-blind method for 4 weeks in 56 hospitalized geriatric patients who had behavioral symptoms associated with senility. Clinical assessment was made by the psychiatrists' modified Hamilton Anxiety Scale for specific psychiatric symptoms and by the Nurses' Observation Scale for Inpatient Behavior (NOSIE) with a global rating for each. On the Hamilton Scale, the thioridazine patients improved more than the diazepam patients with regard to anxiety, tension, fears, behavior at interviews, overall mental illness and global change, whereas the diazepam patients improved more with regard to insomnia, intellect, depressed mood and agitation. The NOSIE ratings favored thioridazine. The only side-effects observed were drowsiness during the first week in 2 thioridazine patients receiving 60mg daily and in 4 diazepam patients receiving 18mg daily; one of the diazepam patients also had slurred speech for the first week. The conclusion is that in the relatively low dosage employed in this series, thioridazine will improve behavioral symptoms in senile patients without the added stress of oversedation or other side-effects. 9 references. (Author abstract)

170292 Levine, Jerome; Lipman, Ronald S. Psychopharmacology Research Branch, Div. of Extramural Research Programs, NIMH, 5600 Fishers Lane, Rockville, MD 20852 **Psychotherapeutic drug trials among English general practitioners.** In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 79-84).

Psychotherapeutic drug trials were carried out among English general practitioners when it was determined that the general practitioners and internists prescribe the majority of drugs associated with psychiatric disorder. A group of 400 practi-

tioneers carry out research on the use of psychotropic drugs in general practice. It is felt that older drugs would be preferred to newer drugs until there is evidence to support the therapeutic superiority of the new agent; phenobarbital, dextroamphetamine and a dextroamphetamine barbiturate combination were tested. The new drug chlordiazepoxide (CDP) was tested against phenobarbital and newer antianxiety drugs were compared to CDP; patients who respond well to drugs were compared to those who do not. Other topics studied include the treatment of enuresis in children; the use of psychotherapeutic drugs in the treatment of menopausal symptoms and in the distress experienced by peptic ulcer patients; and the possible role of psychiatric symptomatology in cases of essential hypertension. Nonmedical aspects of the research -- cost, drug trials, funding and advantages -- are discussed.

170293 Lehmann, Heinz E.; Ban, Thomas A. Dept. of Psychiatry, McGill Univ. Medical School, Montreal, Quebec, Canada **Megavitamin treatment, culture and tranquilizers, drugs for the aged: projects of a Canadian grant.** In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 85-93).

Selected activities of a group of Canadian researchers into megavitamin treatment, culture and tranquilizers, and drugs for the aged are reported. The following studies are detailed: the use of nicotinic acid in the treatment of schizophrenia with generally negative results; two controlled studies of psychoneurotic patients in which the antidepressant drug doxepin was compared to chlordiazepoxide for French speaking and English speaking patients with differing results; and the prediction of therapeutic response in psychogeriatrics with the use of six psychoactive drugs. 5 references.

170412 Setyonegoro, R. Kusumanto; Tjandra, J. Dept. of Psychiatry, Univ. of Indonesia, Faculty of Medicine, Salemba 6, Djakarta, Indonesia **Trial of oxazepam in ambulatory psychoneurotics.** Indonesian Psychiatric Quarterly (Djakarta). 4(3):49-57, 1971.

The effect of Oxazepam was studied in 200 Indonesian ambulatory psychoneurotic outpatients. Oxazepam was introduced at a low dosage: one 15mg capsule once per day. The maximal level was nine 15mg capsules per day; this dosage was utilized in only seven patients. Treatment was maintained for 4 or 5 weeks. Most of the problems encountered fell into the categories of either psychophysiologic reactions, anxiety reactions, mixed psychoneuroses, or neurotic depressive reactions, and the degree of clinical improvement generally followed in that order. Moderate and marked improvement occurred in 75% of all patients. Relief of anxiety was the most characteristic effect of this agent. Where problems other than anxiety predominated, as in neurasthenia, chronic insomnia, or obsessive compulsive states, oxazepam tended to be much less effective. Clinical improvement was inversely related to the dosage level. Most patients found the treatment satisfactory and expressed the desire to remain on a maintenance regimen. This was permitted, usually at the level of one capsule (15mg), two or three times daily. Side-effects were minimal. 24 references.

170413 Winaktu, O. A. Dept. of Psychiatry, Faculty of Medicine, Univ. of Indonesia, Djakarta, Indonesia **Experiences with laroxyl (R) in the treatment of depressions in private psychiatric practice in Djakarta.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):254-259, 1970.

The effects of the psychotropic drug Laroxyl on a mixed diagnostic group of 122 ambulatory and/or hospitalized mental patients, selected for severe depression, are discussed. Normal dosage was 30 to 45mg per day in divided doses, with an occasional 25mg at night. Improvement occurred in nearly 80% of the patient group. The results in the different diagnostic groups are summarized. Side-effects are also reviewed, including those which required termination of treatment.

170414 Tandou, O. P. Dept. of Psychiatry, Faculty of Medicine, Univ. of Indonesia, Djakarta, Indonesia **Preliminary experiences with nobrium in private psychiatric practice in Djakarta.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):251-253, 1970.

The effect of Nobrium on anxiety was studied in three private psychiatric practices in Djakarta, utilizing 33 Ss aged 17 to 45 years. Only functional neurotic conditions with or without somatization reactions were treated. Those patients with pathological organic conditions and old people, presumptive by their old age of having some organic brain disorder, were not included. Evaluations of the results were made at the end of 4 weeks at the latest to reduce psychotherapeutic interference to a minimum, although no

psychotherapy was done intentionally. The diagnoses included: anxiety reactions, obsessive-compulsive reactions, phobic reactions, depressive reactions, and somatization reactions. The lowest dose given was 5mg, two times a day; the highest dose was 10mg, four times a day. The majority of cases reacted favorably to 10mg, three times a day. Excellent or good effectiveness was obtained in all the patients except one with somatization reactions; his effectiveness rating was fair. Side-effects were encountered in 13 patients and involved: drowsiness, dizziness, and muscle weakness; but they were very mild and disappeared after a few weeks while continuing medication.

170415 Nishizono, Masahisa. Dept. of Psychiatry, Kyushu Univ. School of Medicine, Fukuoka, Japan **On pharmaco-psychotherapy; the role of the psychotherapeutic situation in psychotropic medication.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):246-250, 1970.

The use of psychotropic drugs in different psychotherapeutic milieu is discussed. In one study, chlorprothixene was administered to 30 chronic schizophrenics divided into two groups. One group employed maximum patient - staff interaction, the other no interaction. The former group showed improvement in six patients, the latter in one. It is concluded that combined therapy is necessary in schizophrenics with endogenous psychosis. Levomepromazine combined with psychoanalysis, called anaclitic pharmacopsychotherapy, applied to various types of neuroses has shown good effect, especially in obsessive-compulsive neurosis, character neurosis, borderline schizophrenia, and homosexuality for which a variety of pharmacotherapy or psychotherapy alone did not bring favorable results. A heavy dose of Levomepromazine acts upon the personality of the patient at the physiological level. It affects the instinctive impulse or id function, and weakens its capacity. The defensive function of the ego is also weakened. A change or simplification occurs in the id - ego - superego balance. As the mental structure becomes simplified, the attitude of the patient towards the therapist becomes less complex.

170744 Levine, Fredric M.; Spitalnik, Robert; Dobos, Charles. State University of New York, Stony Brook, NY **Caudate nucleus effects on geriatric senility: effect of belladonna on learning and memory of geriatric patients.** Perceptual and Motor Skills. 37(3):1003-1007, 1973.

Whether a drug could slow caudate activity and thus decrease cortical disruption was investigated. Recent research has raised the possibility that learning and memory losses which characterize geriatric senility may be due to increased activity of the caudate nucleus. Belladonna was unsuccessfully tried as a caudate inhibitor. The results indicated that aging leads to a greater learning loss than loss of memory. 12 references. (Author abstract)

170753 Setyonegoro, R. Kusumanto; Adikusumo, Arman. Dept. of Psychiatry, Faculty of Medicine, Univ. of Indonesia, Salemba 6, Djakarta, Indonesia **Clinical trial with dartalanR, Djakarta, Indonesia.** Indonesian Psychiatric Quarterly (Djakarta). 5(3):76-81, 1972.

The effect of Dartalan, a phenothiazine derivative, on a wide variety of diagnostic categories was studied in 125 patients in Djakarta. The 76 males and 49 females with ages from 14 to 63 years were diagnosed as: simple, hebephrenic, catatonic, paranoid, affective, acute reactive, and unspecified schizophrenics; paranoid, manic, depressive, symptomatic, and involutional psychotics; behavior problems, and other psychosis. Medication started with dosages of one tablet (10 mg) three times a day; increased every 3 to 6 days until an optimal clinical response was obtained. The dosage was maintained for a few weeks, and afterwards reduced gradually. The maximum dosage administered was 60mg/day. In addition, according to necessity, antiparkinson drugs (Cogentin or Artane) were given. The patients' mental status was evaluated through the Brief Psychiatric Rating Scale (BPRS). Twenty six patients showed good improvement (24.3%); 24 patients showed moderate improvement (22.4%); 28 patients achieved slight improvement (26.2%); and 29 patients showed no improvement (27.1%) 18 were considered dropouts. It is concluded that Dartalan can be considered a useful mild tranquilizer. 3 references.

171122 Halpern, B.; Sircovich, O.; Winnik, H. Z. no address **A clinical experiment with sulpiride.** Israel Annals of Psychiatry and Related Disciplines (Jerusalem). 11(2):112-121, 1973.

A clinical experiment with sulpiride, a psychotropic drug which has been used to treat duodenal hyperactivity, various vertigo syndromes, and mental illness is presented. Current research on the drug is summarized and a clinical experiment which was carried out with 23 long-

term patients is described. It is concluded that the drug affected psychomotor and effective arousal, which enabled social recovery. The antipsychotic effect was also marked, although it occurred less often and was more distinct when sulpiride was administered in conjunction with phenothiazine. 8 references. (Author abstract modified)

171150 Maramis, W. F. Division of Psychiatry, Department of Neurology and Psychiatry, Medical Faculty, Airlangga University, Surabaya, Indonesia **A trial on bromazepam (Lexotan) and placebo in the treatment of psychophysiological disorders.** Asian Journal of Medicine (Hong Kong). 9(11):387-389, 1973.

A double-blind crossover trial on bromazepam versus placebo was done in the treatment of patients with predominant psychophysiological symptoms on an ambulatory basis. Bromazepam did much better than placebo, with a decrease in the average morbidity score. Bromazepam scores were better for the semantic than for the psychic symptoms. Minimal undesirable concomitant effects were found. Bromazepam may be of valuable help in the treatment of patients with psychophysiological disorders. 5 references.

171246 Maruko, Kazuo; Ishige, Kyoko; Takaya, Yuzo; Yashima, Yuko. Department of Neuropsychiatry, Fukushima Medical College, Japan **Paroxysmal right-left disorientation in an epileptic patient.** Clinical Psychiatry (Tokyo). 14(10):935-939, 1972.

A case of epilepsy with paroxysmal right - left disorientation is discussed. The patient was a 20-year-old male who experienced the first generalized epileptic seizure at age 15 years. During the seizure, the patient was unable to distinguish between right and left, experienced visual disturbance, and finally developed tonic cramps which changed to myoclonia and gradually disappeared. Bemegride (65 mg) activated the onset of spike and wave complex predominantly at the left parietal and occipital areas and at the same time activated onset of proxysmal right - left disorientation. 17 references.

171282 Nishida, Kohei; Namba, Tsunehiko; Tsutsui, Sueharu; Abe, Tatsuo. School of Medicine, Toho University, Japan **A double-blind clinical trial of doxepin hydrochloride and diazepam in psychosomatic disease, neurosis and depression in the field of internal medicine.** Journal of Japanese Psychosomatic Society (Tokyo). 12(4):36-46, 1972.

The effects of doxepin and diazepam on psychosomatic diseases, neuroses and depression are compared, based on a double-blind test in which 28 patients with psychosomatic diseases, 22 with neuroses and 22 with depression were treated with doxepin (20 to 40mg/day for 3 weeks) or diazepam (4 to 8mg/day for 3 weeks). Of 25 matched pairs completing the test, doxepin was superior to diazepam in 8 pairs and inferior to diazepam in 11 pairs and equal to it in 6 pairs, which indicates no significant difference in the two drugs. Among 32 patients treated with doxepin, 20 showed marked or moderate clinical improvement, and among 28 patients treated with diazepam, 19 showed the same degree of improvement, which indicates that the two drugs have almost the same effect on psychosomatic diseases, neuroses and depression. Twelve patients dropped out of this drug test, four on doxepin and eight on diazepam. No significant side-effects were observed. 13 references. (Author abstract modified)

171496 Guilleminault, Christian; Carskadon, Mary; Dement, William C. Sleep Disorders Clinic and Lab., Stanford Univ. School of Medicine, Stanford, CA 94305 **On the treatment of rapid eye movement narcolepsy.** Archives of Neurology. 30(1):90-93, 1974.

Fifty patients were diagnosed as having rapid eye movement (REM) narcolepsy by means of polygraphic recordings. The effectiveness of amphetamine and tricyclic antidepressant drugs on the classical symptoms of REM narcolepsy were considered. Side-effects developed with each of these medications. Imipramine hydrochloride and clomipramine hydrochloride appear to be effective for cateplexy, sleep paralysis, and hypnagogic hallucinations, but there is no effective and harmless treatment for daytime sleep attacks. (Journal abstract)

172272 Janowsky, David S.; El-Yousef, M. Khaled; Davis, John M.; Sekerke, H. Joseph. Department of Psychiatry, School of Medicine, University of California at San Diego, P.O. Box 109, La Jolla, CA 92037 **Antagonistic effects of physostigmine and methylphenidate in man.** American Journal of Psychiatry. 130(12):1370-1376, 1973.

The antagonistic effects of physostigmine, a centrally acting acetylcholinesterase inhibitor, and methylphenidate, an amphetamine like stimulant, on manic and schizophrenic aptients are

described. In both patient groups, physostigmine increased behavioral inhibition and decreased behavioral activation; patients displayed symptoms that are characteristic of psychomotor inhibition. Methylphenidate had the opposite effect of increasing activation and decreasing inhibition. Treatment with each drug antagonized the effects of the other. In the schizophrenic patients, physostigmine prevented and reversed the methylphenidate induced symptoms of psychosis. In manic patients, physostigmine decreased and methylphenidate increased manic symptoms. 28 references. (Journal abstract modified)

172275 Rothstein, Emil. Alcoholism Unit, Veterans Administration Hospital, Brockton, MA 02401 **Prevention of alcohol withdrawal seizures: the roles of diphenylhydantoin and chlordiazepoxide.** American Journal of Psychiatry. 130(12):1381-1382, 1973.

Two hundred patients with histories of chronic alcoholism and recent bouts of heavy and uncontrolled drinking were treated for alcohol withdrawal symptoms through the use of chlordiazepoxide and thiamine. One hundred of these patients, chosen at random, also received diphenylhydantoin. No withdrawal seizures occurred in either group, nor were any other differences observed. Patients with a history of previous withdrawal seizures were included in both groups. These observations suggest that when adequate doses of chlordiazepoxide and thiamine are used during alcohol withdrawal, no additional anticonvulsant drug is needed to prevent seizures. 8 references. (Author abstract)

172439 Singhal, B. S.; Hansotia, P.; Parekh, C. S.; Hawaldar, P. P. Department of Neurology, Medical Research Center of the Bombay Hospital Trust, Bombay, India **Study of the psychotropic action of Tegretol in patients with epilepsy.** Bombay Hospital Journal (Bombay). 14(2):41-47, 1972.

Tegretol, as a psychotropic agent and anticonvulsant drug, is evaluated and compared to other anticonvulsant drugs. Tegretol was administered to 24 patients with epilepsy and behavior changes. Complete control of epilepsy was achieved in four patients, 75% reduction in eight patients, 50% reduction in seven patients, and 25% reduction in two patients, with three remaining unchanged. Psychiatric improvement was noted in 10 patients, with four out of 15 having improved motor coordination. No serious side-effects were encountered. It is concluded that the psychotropic action of the drug and relative freedom from side-effects make Tegretol a useful anticonvulsant drug. 16 references. (Author abstract modified)

172512 Zara, Martha M. Northern Illinois University **Effects of medication on learning in hyperactive four-year-old children. (Ed.D dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-27620 HC$10.00 MF$4.00 53 p.

The effectiveness of two training procedures, passive movement training and vicarious imitation training, on a perceptual motor task and its reversal by medicated hyperactive minimal brain dysfunction (MBD) 4-year-old children was studied. Significant interaction conditions by task indicated that subjects in the never drug condition had developed verbal control of nonverbal behavior as measured by the perceptual motor task and its reversal, while on drug and off drug subjects had failed to develop verbal control of nonverbal behavior. It is suggested that the hyperactive MBD subjects who had been receiving stimulant drug therapy, and who were examined in either the on drug or off drug condition, exhibited a cognitive inflexibility that was not exhibited by those who had never been medicated. Recommendations for further research are given. (Journal abstract modified)

172615 Freemon, Frank R. no address **Sleep research. A critical review.** Springfield, IL, Charles C Thomas, 1972. 205 p. $14.50.

Sleep research (the basic science, clinical aspects, and theories) is reviewed. The two types of sleep and their various substages are reviewed, and particular data are given which apply to adults and infants. Various studies on mental activity during both types of sleep and their relation to psychoanalytic dream theory are examined. Physiology and neurochemistry of sleep from animal studies involving macroelectrode and microelectrode recordings and the use of lesions and pharmacological agents are examined. The sleep of man and chimpanzees are compared. Total (rapid eye movement (REM) and non-REM) sleep or REM sleep deprivation and the biochemical changes which would occur in the neurotransmitters, chemical and enzymatic constituents, and energic processes are examined. The discussion on arousal covers the ascending reticular activating system and the control of sensory input and environmental interaction. Clinical pharmacology of sleep, sleep disorders, and sleep in the

pathophysiology of medical and neurological diseases are covered. (Journal abstract modified)

172800 Tongyonk, John. Bangkok Medical and Pediatric Clinic, Bangkok, Thailand **Hyperkinetic, hyposcholastic behaviour and character disorders of childhood and adolescence: diagnosis and pharmacotherapy.** Journal of the Psychiatric Association of Thailand (Bangkok). 15(3):228-242, 1970.

Hyperkinetic, hyposcholastic behavior and character disorders of childhood and adolescence, particularly their diagnosis and pharmacotherapy, are discussed. Only extensive anamnesis and correct clinical examination lead to etiological diagnosis and effective treatment. Disorders discussed include: hyperactivity, defects of attention, excitability, learning disabilities, and neurological concomitants. Clinical assessments include: neurological, behavioral, sociofamilial - environmental, and psychoeducational assessment. Aspects of differential diagnosis are treated. Drug therapy includes treatment with amphetamines and methylphenidate, barbituates, tranquilizers, phenothiazines, butyrophenones, meprobamate and the chlordiazepoxide series, and vitamins. 131 references. (Author abstract modified)

172834 Moore, Robert A. Mesa Vista Hospital, San Diego, CA **Psychotherapeutics of alcoholism.** Alcohol Health and Research World. Fall:20-23, 1973.

The psychotherapeutics of alcoholism are discussed, based on the way many psychiatrists treat alcoholism today. Characteristics of the patient population are summarized. The patient is employed or at least partially financially solvent, lower-middle-class and up. Treatment is covered by private funds or health insurance or is provided in a public clinic. A recent study of private psychiatric hospitals reveals that alcoholics make up 11% of all admissions. Patients appear to be sociable and jolly, but are lonely and unrelating. Treatment in group therapy is reviewed. The focus of the groups is to attack the denial system and to confront patterns of behavior in the hospital. The use of antabuse is encouraged. Alcoholism is not seen as a disease to be cured, but rather as a serious and chronic defect in living. 30 references.

172977 Zaragoza, H.; Burner, M. no address **/The use of timed release neuroleptics in ambulatory psychiatric practice./** Utilisation des neuroleptiques-retard en pratique psychiatrique ambulatoire. Medecine et Hygiene (Geneve). No. 29:975-978, 1971.

Results of a detailed study of the treatment of 80 patients with fluphenazine enanthate, fluphenazine decanoate, and flupenthixol decanoate are described. Treatment with the enanthate lasted from 12 to 15 days, that with fluphenazine decanoate and flupenthixol decanoate for 4 weeks. Dosage is listed. Fluphenazine enanthate treatment resulted in a few cases of neurodysleptic crises and a depressive syndrome. Fluanxol had no sedative effect. The fluphenazine decanoate had fewer side-effects than the enanthate form. Fluphenazine forms are indicated for acute cases when sedation from an agitated state is desired. Fluanxol is reserved for nonagitated patients who need stimulation.

172980 Rosier, Y. A.; Moreau, D. no address **/The corrective effect of Praxinor on hypotension attributable to psychiatric therapy. Side-effects./** Correction par le Praxinor des hypotensions dues aux therapeutiques psychiatriques. Cahiers Medicaux Lyonnais (Lyon). No. 47:979-981, 1971.

The drug Praxinor (Akrinor in Belgium) is described as a mixture of two xanthic derivatives, the enzymatic degradation products of which are theophylline and circulatory analeptics in an amino - ethanol fraction. The pharmacological action is to reinforce the tonus venous and increase myocardiac contractability without peripheral vasconstriction. An average dose of four tablets a day corrects secondary hypotension caused by psychopharmacological treatments. No counterindication with MAOI is noted. Praxinor has the additional property of being able to increase awareness.

173190 Bazo, Albert J. Fairlington Professional Bldg., 1707 Osage St., Alexandria, VA 22302 **An ergot alkaloid preparation (Hydergine) versus Papaverine in treating common complaints of the aged: double-blind study.** Journal of the American Geriatrics Society. 21(2):63-71, 1973.

Results of a double-blind study in which 66 geriatric patients with various common complaints of the aged, attributable to cerebral arteriosclerosis with cerebrovascular insufficiency received standard dosages of Hydergine or papaverine for 12 weeks, are presented. Ratings of symptom severity, overall clinical condition, global therapeutic change, and mental status evaluations

show that the Hydergine group consistently improved more than the papaverine group. The greatest benefits of Hydergine therapy seemed to be in the areas of intellectual function or cognition. 18 references. (Author abstract modified)

173205 Wolcott, George J.; Chun, Raymond W. M. Department of Neurology, University of Wisconsin Center for Health Sciences, 1300 University Avenue, Madison, WI 53706 **Myoclonic seizures in Down's syndrome.** Developmental Medicine and Child Neurology (Tadworth, Surrey, England). 15(6):805-808, 1973.

Three children with Down's syndrome are reported with spontaneously occurring myoclonic seizures. Electroencephalograms were markedly abnormal, but improved after medication in two cases. Seizures were controlled with drugs in two of the children, but were not well controlled in the third, despite attempts with several types of medication. The etiology of these myoclonic seizures remains unclear. 12 references. (Author abstract)

173433 Mason, Aaron S. Veterans Administration Hospital, Downey, IL **Basic principles in the use of antipsychotic agents.** Hospital & Community Psychiatry. 24(12):825-829, 1973.

Basic principles in the use of antipsychotic agents are discussed. It is suggested that after 17 years of extensive use in treating psychoses, antipsychotic agents are still inappropriately prescribed by psychiatrists and other physicians. A set of clearly defined principles of drug administration are presented. It is concluded that the mastery of these basic principles will lead to the skill and expertise necessary to use the drugs in the most effective and economical manner. 10 references. (Author abstract modified)

174044 Bobon, J.; Bourdouxhe, S.; Breulet, M.; Parent, M.; Bobon, D. P. Clinique psychiatrique universitaire, Rue St-Laurent, 58, B-4000 Liege, Belgium **Pilot clinical trial of parenteral lorazepam (Temesta) in anxiety states.** Psychopharmacologia (Berlin). 33(4):377-384, 1973.

The effects of IM and IV lorazepam were studied in an open trial and in a double-blind cross over trial in 13 and 15 adult patients respectively, all being inpatients suffering from psychic and somatic manifestations of anxiety. At a mean dosage of 5 mg t.i.d.,lorazepam proved significantly superior to placebo in the treatment of acute anxiety as well as in chronic anxiety states. The side-effects were minor; the main one was decreased wakefulness. The local and the biological tolerance were excellent. 5 references. (Author abstract)

174071 Yang, Dorthy C.; Fisch, Martin L.; Lamm, Stanley S. Children's Center for Developmental Disorders, Long Island College Hospital, 340 Henry St., Brooklyn, NY 11201 **Rehabilitation of learning in a hospital class using psychoactive drugs.** Journal of Learning Disabilities. 6(8):486-491, 1973.

Through the combined efforts of the educational and health care professionals in a hospital based outpatient special class, a unique environment was provided for children with learning disabilities. Eight children who were uncontainable in public schools showed improvement in four semesters in a special class. Procedures emphasized daily intercommunication between the educators and the staff, enabling modification in progress to be made constantly. Drugs were used to help the children to be more receptive to learning. Both Ritalin and Dexedrine decreased distractibility, irritability, silly behavior and overactivity. 1 reference. (Author abstract modified)

174298 Thornton, William E.; Thornton, Bonnie Pray. 848 First Ave. North, Naples, FL 33940 **Crisis psychopharmacology techniques.** Diseases of the Nervous System. 35(1):32-34, 1974.

The need and effectiveness of crisis psychopharmacology techniques are discussed in terms of both immediate goals and long range benefits in improving patient attitude and confidence. It is found that the acute psychiatric patient often responds to immediate high doses of phenothiazines, which may be potentiated by the addition of a barbiturate. Depression is felt to be a commonly missed diagnosis and is generally very susceptible to chemotherapy. In resistant patients, the administration of higher doses or of potentiating agents often yields desired results. Acute anxiety is distinguished by its susceptibility to the milder, less hazardous sedatives and minor tranquilizers, whose hypnotic effects are recommended in the initial treatment. 16 references. (Author abstract modified)

174568 Thong, Y. H.; Abramson, David C. Department of Pediatrics, Georgetown Univ. School of Medicine, Washington, DC 20007 **Continuous infusion of diazepam in infants were severe recur-**

rent convulsions. Medical Annals of the District of Columbia. 43(2):63164, 1974.

The use of diazepam by intravenous infusion in five pediatric patients with severe convulsions secondary to acute cerebral insults is examined. Case reports and diagnostic assessments of all five patients are presented along with dosage levels and duration of dosage information. Results indicate that this mode of therapy is both safe and effective in controlling refractory seizures and successfully prevents their recurrence. Effective levels of diazepam for the control of severe recurrent convulsion in this series ranged from three to twelve mg/kg/day. Toxic manifestations attributable to diazepam were not observed. Respiratory depression was not encountered in any of the patients, all of whom had received multiple doses of anticonvulsants prior to institution of this mode of therapy. 21 references. (Author abstract modified)

174783 Kedzior, Janusz; Nowakowski, Henryk. Szpital Wojskowy, Elblag, ul. Komenskiego 35, Poland /**A case of encephalitis with psychotic complications.**/ Zapalenie mozgu z powiklaniem psychotycznym. Psychiatria Polska (Warszawa). 7(2):215-218, 1973.

A case of encephalitis in a 33-year-old married woman admitted to the psychiatric department of a hospital with the diagnosis of catatonic paranoid syndrome is detailed. The inflammatory nature of the disease was recognized during hospitalization and treatment involving 20% mannitol, tetraverin, penicillin, hydrocortisone, Orisul Ciba, and haloperidol was prescribed. The inflammation was cleared up but the mental defects will require a long period of rehabilitation with physiotherapy indicated. Similar cases, in which the diagnosis of encephalitis was made difficult because of the mental symptoms present, are discussed in brief. 5 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

168420 Jaffe, J.; Dahlberg, C. C.; Luria, J.; Chorosh, J. Department of Communication Sciences, New York State Psychiatric Institute, 722 West 168 Street, New York, NY **Effects of LSD-25 and dextroamphetamine on speech rhythms in psychotherapy dialogues.** Biological Psychiatry. 6(1):93-96, 1973.

The effects of LSD-25 and dextroamphetamine (DA) on speech rhythms in psychotherapy dialogues were investigated and compared to those found for monologues. Pause duration is one major mechanism by means of which speech rate is controlled. Findings generally replicated monologue results, confirming the hypothesized effect that with respect to a placebo, the average pause duration was lengthened by LSD and shortened by DA, whereas mean vocalization duration was not significantly affected. 6 references.

173522 Kaplan, Jonathan; Stillman, Richard; Wyatt, Richard. Laboratory of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **DMT administration to human subjects. (Unpublished paper).** Washington, DC, NIMH, 1973, 1 p.

The effects of N,N-dimethyltryptamine (DMT) were examined to determine if this could be considered a model for a psychotic reaction. Within 90 to 150 minutes of injection, subjects began experiencing psychic changes. The most striking effects were visual perceptual changes. There was an increase in color intensity, more pronounced depth sensations, and a sense of movement in the surroundings. When Ss closed their eyes they saw colored geometric patterns rather than formed hallucinations. Physiologic changes which paralleled the time course of the psychic changes were an increase in systolic and diastolic blood pressure, a small increase in pulse rate, and pupillary dilatation. It was found that patients who denied changes in cognition or perception still did poorly on perceptual motor tasks while on the drug. Ten minutes after drug administration the blood level was 160ngm/ml, at 20 minutes the level remained 160, at 1 hour it had dropped to 20ngm/ml and at 2 hours 1.7ngm/ml. (Author abstract modified)

174480 Bell, J. A.; Martin, William R. NIMH Addiction Research Center, P.O. Box 2000, Lexington, KY 40507 **The effect in the cat of tryptamine (T) and LSD on cutaneous C-fiber (CFR) and polysynaptic (PSR) spinal reflexes. (Unpublished paper).** Lexington, Ky., NIMH Addiction Research Center, 1973. 1 p.

The effect in the cat of tryptamine (T) and lysergic acid diethylamide (LSD) on cutaneous C-fiber (CFR) and polysynaptic (PSR) spinal reflexes was investigated. The facilitation by T was antagonized by cyproheptadine (C) 0.5mg/kg. LSD, infused at a rate of 0.375mcg/kg/min for 40 minutes, produced a facilitation of the CFR which reached a maximum 60 minutes postinfusion. Facilitation of the PSR by LSD was significant

only immediately postinfusion. Facilitation of the CFR by LSD was partially antagonized by C (0.5mg/kg). In T experiments, methysergide (M) was administered over a 20 minute period. The CFR was initially depressed following M but increased to above control level 30 minutes after M in 4 to 7 experiments. T produced a significant depression of CFR after M. These studies demonstrated that T and LSD have a similar mode of action on spinal cord CFR's, and that the CFR is more sensitive to the actions of T and LSD than is the short latency PSR. (Author abstract modified)

174496 Kay, D. C.; Martin, W. R.; Croughan, J. L. NIMH Addiction Research Center, P.O. Box 2000, Lexington, KY 40507 **EEG and cardiovascular effects of tryptamine (T) and LSD in the encephale isole cat. (Unpublished paper)** Lexington, Ky., NIMH Addiction Research Center, 1973. 1 p.

The electroencephalogram (EEG) and cardivascular effects of replicate 2 minute intravenous infusions of tryptamine (T) (0.5mg/kg/min) administered at a mean interval of 63.1minutes were studied in 6 encephale isole cats. T significantly reduced absolute power of delta and alpha activity, with a late increase in beta activity. The pattern of effects on theta activity were not consistent. T also increased blood pressure and pulse rate. The effects of replicate 5 minute infusions of lysergic acid diethylamide (LSD) administered at a mean interval of 67.5minutes were studied in another 6 cats. LSD significantly decreased delta and theta activity, and produced no significant cardiovascular effect. Delta and theta activity were only slightly decreased. Both LSD and T produce a modest EEG synchronization at the reported doses. (Author abstract modified)

174605 Sankav, D. V. Sira; Kumbar, Mahadevappa. Queen's Children's Hospital, Bellerose, NY 11426 **Quantum chemical studies on drug actions: IV. correlation of substituent structures and anti-serotonin activity in lysergamide series.** Research Communications in Chemical Pathology and Pharmacology. 7(2):259-274, 1974.

The correlation of quantum parameters of the lysergates with the antiserotonin activity of derivatives of LSD-25 is studied. Several hypotheses have been put forward relating the structures of LSD-25 and its congeners to the indolyl structure of tryptamines, and especially serotonin. The importance of side chain structures of the lysergates is stressed. The antiserotonin activity of several lysergate derivatives seems to be dependent on the total orbital energy, but not on the HOMO energy of the molecule. The logarithm of hallucinogenic activity is related to the logarithm of antiserotonin activity. A high degree of electron delocalization over the entire ring structure is suggested, indicating possible resonance leading to effectual partial pi bonding between all four rings. The universal importance claimed for HOMO energy cannot be considered valid in the light of these studies. 18 references. (Author abstract modified)

174606 Dunn, William J., III; Bederka, John P., Jr. College of Pharmacy, Univ. of Illinois at the Medical Center, 833 S. Wood, Chicago, IL 60680 **The role of hydrophobicity in the antiserotonin activity of LSD analogs.** Research Communications in Chemical Pathology and Pharmacology. 7(2):275-285, 1974.

Published data on the anti-5HT activities of a series of LSD analogs are analyzed. An attempt is made to determine parameters common to the hallucinogenic potencies of LSD analogs and their antiserotonin activities. Analysis is done within the framework of the Hansch model for quantitative structure activity relationships using the 1-octanol/water partition coefficient as a model for lipophilicity and other linear free energy based parameters as variables in the correlations. Results indicate that the hydrophobicity of the amide substituents, when this is the variable portion of the molecule, is important in determining the anti-5HT potency. A relationship between physiochemical properties and activity could not be found in analyzing the limited data on hallucinogenecity in man. 18 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

167336 Arrigo, A.; Braun, P.; Kauchtschischwili, G. M.; Moglia, A.; Tartara, A. Clinic of Nervous and Mental Diseases, Univ. of Pavia, Italy **Influence of treatment on symptomatology and correlated electroencephalographic (EEG) changes in the aged.** Current Therapeutic Research. 15(7):417-426, 1973.

A 12 week, double-blind study of 20 elderly patients suffering from cerebral vascular insufficiency was made to compare the therapeutic effects

of Hydergine and placebo. A positive correlation between clinical improvement and reorganization of the electroencephalogram tracing under treatment with the active substance was established. Placebo had little effect. The medication was well tolerated and no side-effects were reported. 16 references. (Journal abstract modified)

167460 Teoh, P. C.; Cheah, J. S. Department of Medicine (Unit 1), University of Singapore, Sepoy Lines, Singapore 3 **Electrocardiographic changes in hyperthyroidism after adrenergic blockade with reserpine and propranolol.** Medical Journal of Australia (Syndey). 2(3):116-118, 1973.

Electrocardiogram changes in 15 hyperthyroid patients' treatment with reserpine and propranolol are reported. The findings support the concept that the tachycardia in hyperthyroidism is caused partly by the direct action of the thyroid hormone on the myocardium and partly by increased sensitivity to the catecholamines, whereas the other electrocardiographic changes are mainly due to the direct action of thyroid hormone on the myocardium. As both reserpine and propranolol block the action only of catecholamines at the adrenergic receptors and do not in any way interfere with the production of thyroid hormones, they do not correct the cardiac abnormalities due to direct action of thyroid hormones. 10 references. (Author abstract modified)

167584 McClure, D. J. Faculty of Medicine, McGill University, Montreal, Quebec, Canada **The role of dopamine in depression.** Canadian Psychiatric Association Journal (Ottawa). 18(4):309-312, 1973.

The possible role of dopamine (3, 4-dihydroxyphenylethylamine) an important catecholamine, in the affective disorders is discussed. A review of the literature is presented, and it is concluded that, although the role dopamine plays in the pathogenesis of depressive iilness is still unknown, it appears to be an important one. 31 references.

168286 Sandler, M.; Carter, Susan Bonham; Hunter, K. R.; Stern, G. M. Bernhard Baron Memorial Research Laboratories, Queen Charlotte's Maternity Hospital, London, W6 OXG, England **Tetrahydroisoquinoline alkaloids: in vivo metabolites of L-Dopa in man.** Nature (London). 241(5390):439-443, 1973.

Tetrahydroisoquinoline alkaloids were unequivocally demonstrated in vivo for the first time in parkinsonian patients on L-Dopa treatment. The identification, in significant concentration of two of the alkaloids, salsolinol and tetrahydropapaveroline, in the urine of patients under oral L-Dopa treatment is reported, as determined by mass spectrometric studies. Their biosynthesis may have a profound bearing on how L-Dopa acts. Findings with these patients, when considered in light of biochemical research in schizophrenia, suggest that study of tetrahydroisoquinoline metabolism in schizophrenics might be rewarding. It is also possible that another type of mental disorder, phenylketonuria, originates from the disproportionate presence of a carbonyl agent, phenylpyruvic acid, which may form a complex with a biogenic amine such as dopamine. 34 references.

168578 Benvenuti, P.; Binazzi, A.; Pazzagli, A.; Amaducci, L. Clinica delle Malattie Nervose e Mentali, dell-Universita di Firenze, Florence, Italy **/Psychometric investigations in Parkinson's Syndrome during treatment with L-dopa and relevance of some psychological phenomena./** Indagine psicometrica nelle sindromi Parkinsoniane in corso di trattamento con L-dopa (sul significato di alcuni sintomi psichici nel morbo di Parkinson). Rivista di Patologia Nervosa e Mentale (Firenze). 93(4):203-213, 1972.

Psychometric investigations administered to 30 Parkinson patients undergoing treatment with L-dopa are reported. The tests were given at the beginning of therapy and once the maintenance dose had been reached and included: the MMPI, MPI, Cattell's IPAT, a scale for the evaluation of anxious/depressive syndromes (Gainotti and Cianchetti) and some WAIS performance and verbal subtests in order to detect any changes in mood and in certain personality parameters. A statistical analysis of the data showed that significant changes occurred in the MMPI (Es scale), the WAIS subtests and in particular the scale for anxious/depressive symtomatology, especially in the parameters of the basic components of depression (depressed mood, sense of guilt, suicide tendency, loss of interest). It is suggested that the improvement in the depressive state of Parkinson's patients may be related to the direct action of L-dopa. At present, however, it is not possible to determine whether this may take place through a change in catecholamine concentration or other biogenic amines in the CNS. 25 references. (Author abstract modified)

168777 Paulson, George W. Ohio State University College of Medicine, Columbus, OH **Failures of L-dopa.** Ohio State Medical Journal. 69(12):896-898, 1973.

Selected examples of failures in the use of L-dopa are reviewed, and suggestions are offered to lessen the frequency and impact of such therapeutic misadventures. Case summaries are presented which illustrate inappropriate use and prescription of the drug, complications of aging as a reason for failure of the medication, the development of depression, progression of parkinsonism in patients treated with the drug, and its dyskinetic side effects. Despite instances of failure with this medication, L-dopa remains the drug of choice for the treatment of parkinsonism. Because of possible failure, the physician must attempt a realistic appraisal and must be willing to try additional measures.

168802 Silvestrini, B.; Lisciani, R. Research Laboratories, Aziende Chimiche Riunite Angelini Francesco, Rome, Italy **Pharmacology of trazodone.** Current Therapeutic Research. 15(10S):749-754, 1973.

A rationale for the clinical use of trazodone based on pharmacological evidence is presented. Like neuroleptics, trazodone seems to act with humoral type psychotropic mechanisms and fails to show nonspecific depressant actions on the central nervous system. Trazodone differs from other psychotropic drugs in that it acts with unusual selectivity in those conditions which are characterized by the activation of mechanisms of emotional integration of unpleasant experiences. Depression was considered the most demanding field in which to assess the validity of the pharmacological interpretation of the drug but other therapeutic fields like psychoneurosis and surgical premedication should be considered equally inportant. 20 references. (Author abstract modified)

168975 Criscuoli, P. M.; Eliseo, M. Cattedra di Neuropsichiatria Infantile dell'Universita di Palermo, Italy /**Clinical and electromyographic research concerning treatment of peripheral neuropathies with Nivalasi.**/ Ricerche cliniche ed elettromiografiche nelle neuropatie periferiche trattate con Nivalasi. Pisani (Palermo). 94(1-3):233-241, 1970.

Past use of galanthamine (Nivaline), and results obtained, are discussed in brief to show that the drug accelerates the regenerative processes of the sciatic nerve, promoting recovery of its motor functions. Use of Nivalasi, the Italian counterpart, is discussed and clinical evaluation of its use on 23 patients ranging in age from 4 to 13 at the Children's Neuropsychiatric Clinic of the University of Palermo is presented. Cases are tabulated and electromyograms presented. Rationale for posology is stated. Electroencephalographic tracings remained within normal limits and the electromyographic studies confirmed the efficacy of the treatment as demonstrated in the laboratory. 11 references.

169068 Volavka, J.; Crown, P.; Dornbush, R.; Fink, Max. Department of Psychiatry, New York Medical College, New York, NY **EEG, heart rate, and mood change ('high') after cannabis.** Psychopharmacology Bulletin. 9(4):26-27, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the relationship between electroencephalogram (EEG), heartrate, and the mood changes of 'high' and 'pleasantness' following three cannabis preparations - marihuana leaf, hashish, and synthesized delta9-tetrahydrocannabinol (THC) - was discussed. A 10 minute sample of EEG and electrocardiogram (ECG) was taken before smoking in each session. ECG was recorded during smoking and then together with EEG for 50 minutes after the termination of smoking. All cannabis preparations caused an increased in heartrate. This increase was significant throughout the observation period (including the smoking time). 'High' was positively related to the amount of alpha activity as measured by the broad band analysis. This relationship was significant in the first 20 minutes after smoking. On the average, up to 102 beats per minute, heartrate increase was associated with the increase of pleasure. If heartrate increased further, the experience was less pleasurable. (Journal abstract modified)

169070 Frank, Ira M.; Epps, Louise D.; Rickles, William. University of California School of Medicine, Los Angeles, CA **Psychological and physiological effects of chronic marijuana administration in man.** Psychopharmacology Bulletin. 9(4):28-29, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the effects of chronic marihuana administration as determined by the physiological measures of heartrate, blood pres-

sure, respiration, temperature, subjective estimation of 'high', intraocular pressure, water tonography, serum electrolytes, blood chemistries, complete blood count, urinalysis, chest x-rays, bronchial cytology, electrocardiogram, electroencephalogram, pulmonary function tests, and tests for possible chromosomal damage, and by 10 psychological tests were evaluated. Marihuana was found to produce acutely, a dose related increase in heartrate, systolic blood pressure, and the specific conductance of the tracheo bronchial tree, a marked and very consistent dose related decrease in intraocular pressure, and a very slight but consistent increase in pupil size. There was some impairment on mental function tests of mental performance and an elevation of mood. (Journal abstract modified)

169084 Babor, Thomas F. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **/The relationship of marihuana and social behavior./** Studies of group behavior. Psychopharmacology Bulletin. 9(4):51-52, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, an investigation of the relationship between marihuana and social behavior during informal smoking sessions and formal discussion groups was presented. The data indicate very strongly that marihuana smoking in addition to being a subjective drug experience is also a social activity around which verbal interaction and other types of social behavior are centered. Total interaction tended to decrease at higher levels of intoxication, and this relationship was found most consistently in the category of attempted answers. In general, interaction tended to be more positive (agreement and laughter) and less task oriented during intoxication. The findings suggest that while marihuana may be sociogenic in a sociological sense, the psychopharmacological effect of intoxication may actually suppress social behavior by making subjective experiences more salient. (Journal abstract modified)

169091 Schildkraut, Joseph J. Department of Psychiatry, Harvard Medical School, Boston, MA 02115 **Catecholamine metabolism in affective disorders: recent studies of MHPG excretion.** Psychopharmacology Bulletin. 9(4):60-61, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, a longitudinal study of catecholamine metabolism in patients with naturally occurring or amphetamine induced affective disorders (manic and depressive episodes) which indicates that levels of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) are relatively lower during depression and higher during manic or hypomanic episodes than after clinical remissions was reported. Taken in conjunction with pharmacological findings which have suggested an inverse relationship between desynchronized (rapid eye movement) sleep and central catecholaminergic activity, these findings appear to support the view that MHPG excretion may reflect central noradrenergic activity, particularly in patients with manic depressive disorders. (Journal abstract modified)

169377 Chase, Thomas N. Neurology Unit, NIH Clinical Center, 9000 Rockville Pike, Bethesda, MD 20014 **Central monoamine metabolism in man: effect of putative dopamine receptor agonists and antagonists.** Archives of Neurology. 29(5):349-351, 1973.

The effect of haloperidol or piribedil (ET 495) on the central metabolism of dopamine (DA) and serotonin was examined in patients with various neurologic disorders. Monoamine turnover was estimated by the rate of accumulation in lumbar spinal fluid of the principle metabolites of these suspected neuromediators during the administration of probenecid. Haloperidol, which is believed to block DA receptors, appeared to accelerate DA turnover markedly, while piribedil, a suspected DA receptor agonist, substantially reduced the turnover of this monoamine. No consistent change in serotonin metabolism attended the administration of either drug. The results suggest that studies using pharmacologic agents that act on central monoaminergic receptors may provide an important means for evaluating mechanisms for controlling monoamine synthesis in patients with central nervous system disease. 25 references. (Author abstract)

169470 Lewander, Tommy; Sjostrom, Rolf. University of Uppsala, Ulleraker Hospital, S-75017 Uppsala, Sweden **Increase in the plasma concentration of free tryptophan caused by probenecid in humans.** Psychopharmacologia (Berlin). 33(1):81-86, 1973.

The effects of probenecid on the total free concentration of tryptophan in plasma were studied. Probenecid caused an increase by 52% in the free (nonprotein bound) concentration of tryptophan in

plasma. The total (free plus protein bound) plasma tryptophan concentration was not significantly changed by the present dose of probenecid. There was a positive correlation between the increase in percentage free tryptophan and the achieved plasma concentration of probenecid. The cerebrospinal fluid (CSF) concentration of tryptophan was not significantly changed by probenecid given to another group of five patients. It is concluded that the increase in the CSF concentration of 5-hydroxyindoleacetic acid (5-HIAA) caused by probenecid, in addition to blockade of the 5-HIAA transport out of the CSF, might be explained by an increased rate of synthesis of brain serotonin since the availability of its precursor is increased due to the probenecid induced increase in the plasma concentration of free tryptophan. 19 references. (Author abstract modified)

169817 Kaplan, S. A.; de Silva, J. A. F.; Jack, M. L.; Alexander, K.; Strojny, N.; Weinfeld, R. E.; Puglisi, C. V.; Weissman, L. Department of Biochemistry and Drug Metabolism, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Blood level profile in man following chronic oral administration of flurazepam hydrochloride.** Journal of Pharmaceutical Sciences. 62(12):1932-1935, 1973.

The blood level profile of flurazepam and its major metabolites was studied in man following oral administration of 30mg daily for 2 weeks. The levels of the intact drug were below the sensitivity limit of the assay (less than 3-4ng/ml). The hydroxyethyl metabolite was measurable only during the early hours after a 30mg oral dose. The major metabolite in the blood was N-desalkyl-flurazepam, which reached plateau levels after 7 days; its half life of elimination ranged from 47 to 100 hours. 6 references. (Author abstract)

169967 Chase, Thomas N. Neurology Unit, NIMH, Bethesda, MD **Clinical studies of dopaminergic mechanisms. (Unpublished paper).** Bethesda, MD, NIMH, 1973. 21 p.

The effects of haloperidol and piribedil on the central metabolism of dopamine were compared in patients with various neurological disorders. Dopamine turnover was estimated by the rate of homovanillic acid accumulation in lumbar spinal fluid during the oral administration of probenecid. Haloperidol, a blocking agent for dopamine receptors, accelerated dopamine turnover, while piribedil, a suspected dopamine receptor agonist, reduced the turnover of this neuroamine. The magnitude of these changes was substantially smaller in parkinsonian patients than in those with Huntington's chorea. The antiparkinsonian efficacy and toxicity of orally administered piribedil were tested against an inert placebo in idiopathic parkinsonism Ss. At maximum doses (mean 276mg/day) cardinal parkinsonian signs improved by about 30%. The therapeutic efficacy of L-dopa in combination with a peripheral decarboxylase inhibitor was about twice that of piribedil. Adverse effects of piribedil closely resembled those of L-dopa. There was a significant positive correlation between the response to piribedil and L-dopa. Moreover, the amount, but not the percent, of improvement with either drug correlated with the pretreatment severity of parkinsonian signs. 25 references. (Author abstract modified)

170638 Takahashi, Saburo; Okada, Fumihiko; Yamashita, Itaru; Suwa, Nozomi; Kobyashi, Tadashi; Kato, Iwao; Miyamura, Atsuo; Watanabe, Eiichi. Department of Psychiatry and Neurology, Hokkaido University School of Medicine, Japan **The electrocardiographic abnormalities induced by psychotropic drugs.** Clinical Psychiatry (Tokyo). 14(9):807-815, 1972.

Electrocardiographic (ECG) abnormalities in psychiatric patients treated with psychotropic drugs were studied, based on 492 psychiatric patients. Findings are: 267 patients (54.3%) out of the 492 showed abnormal ECG and included 184 patients with schizophrenia, 9 with manic-depression, 4 with neuroses, 10 with epilepsy, 11 with mental retardation, 11 with senile psychosis, 11 with progressive paralysis, 12 with addiction; among the 267, 52 patients had been treated with psychotropic drugs for less than 6 months, 35 for 6 months to 1 year, 20 for 1 to 2 years, 23 for 2 to 3 years, 137 for more than 3 years. A total of 53 patients had circulatory abnormalities prior to psychopharmacological treatment; sinus tachycardia was observed in 89 patients, and myocardial damage in 76; longitudinal studies made of 73 patients showed that 41 patients had aggravated circulatory function, 8 improved, and 24 were unchanged; among 60 patients treated with propranolol, iproveratril, L- Potassium and/or magnesium aspartates, 29 improved circulatory function, 28 were unchanged, and 3 became worse. 26 references.

170660 Takamori, Masaharu; Ishii, Nobuko; Mori, Masataka. First Department of Internal Medicine, Nagasaki University School of

Medicine, 7-1, Sakamoto-cho, Nagasaki, Japan **The role of cyclic 3',5'-adenosine monophosphate in neuromuscular transmission.** Archives of Neurology. 29(6):420-424, 1973.

The neuromuscular transmission defect of the Eaton-Lambert syndrome, in which calcium dependent acetylcholine release by nerve impulse is defective, was partially corrected by epinephrine and methylxanthines. These drugs act on the adenyl cyclase system to increase the content of cyclic 3',5'-adenosine monophosphate (cyclic AMP) in cells and have effects similar to those of calcium. No meaningful change was seen with the drugs in classical myasthenia patients or in normal Ss. Alpha-adrenergic stimulants showed the same action as epinephrine, while the beta-adrenergic stimulants worsened the transmission block. However, the epinephrine induced relief was potentiated by the beta-adrenergic blocker but was eliminated by the alpha-adrenergic blocker. Findings suggest that the presynaptic adrenergic modulation in Eaton-Lambert syndrome is mediated through the alpha receptor. 24 references. (Author abstract)

170662 Ambani, Lalit M.; Van Woert, Melvin H.; Bowers, Malcolm B., Jr. Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06510 **Physostigmine effects on phenothiazine-induced extrapyramidal reactions.** Archives of Neurology. 29(6):444-446, 1973.

The effect of intravenous injection of physostigmine salicylate (1mg) on the extrapyramidal side effects of phenothiazine therapy was investigated in 10 psychiatric patients. Six of the 10 who had developed minimal rigidity or tremor or both during phenothiazine therapy exhibited a worsening of these neurological signs after the physostigmine injection. It is concluded that cholinergic hyperactivity or hypersensitivity, or both, occur in phenothiazine induced Parkinsonism, as well as idiopathic Parkinson disease. 20 references. (Author abstract)

170838 Kaplan, S. A.; Jack, M. L.; Alexander, K.; Weinfeld, R. E. Department of Biochemistry and Drug Metabolism, Hoffmann-LaRoche, Inc., Nutley, NJ 07110 **Pharmacokinetic profile of diazepam in man following single intravenous and oral and chronic oral administration.** Journal of Pharmaceutical Sciences. 62(11):1789-1796, 1973.

Four subjects each received single intravenous and oral 10mg. doses of diazepam and 10mg. orally every 24 hr. for 15 days. The intravenous blood level data were fitted with a three compartment open model system containing both a 'shallow' and a 'deep' peripheral compartment. The 'apparent' half-life of elimination of diazepam following intravenous administration ranged from 21 to 37 hr.,and the calculated volume of distribution ranged from 160 to 205% of body weight. The rate at which diazepam returns to the central compartment from the deep peripheral compartment, k31, was shown to be the rate controlling factor in the elimination of diazepam and in the formation of desmethyldiazepam. Orally administered diazepam was rapidly and completely absorbed. Following chronic administration of 10mg. diazepam every 24 hr.,the minimum and maximum steady state (plateau) levels of diazepam can be successfully predicted or calculated utilizing the pharmacokinetic parameters obtained following intravenous administration. 31 references. (Journal abstract modified)

171007 Reitz, R. H.; Abdallah, A. H.; Roby, D. M.; Krauss, J. A.; Marshall, F. N. Pharmaceutical Section, Chemical Biology Research, Dow Chemical Company, Midland, MI 48640 **Selective antagonism of central nervous system depressants by DH-524; a comparative study with Bemegride.** Proceedings of the Society for Experimental Biology and Medicine. 144(1):291-294, 1973.

DH-524 (2(3,4-dichlorophenoxy)methyl-2-imidazoline), an agent which shares with known analeptics the property of dramatically shortening barbiturate narcosis, is discussed. DH-524 is an agent which antagonizes the effects of some central nervous system depressants, but is without effect upon the narcosis produced by other depressants. This differentiates it from analeptics and stimulants which are nonspecific in their action. DH-524 is further differentiated by its failure to induce convulsions at nonfatal doses and its lack of effect upon spontaneous activity. DH-524 is an effective antagonist at doses which are well tolerated by nonnarcotized animals, while effective doses of bemegride were very toxic to nonnarcotized animals. These data suggest that DH-524 would be more selective and have a wider margin of safety than the commonly used analeptics in the treatment of barbiturate or methaqualone overdose. 6 references. (Author abstract modified)

171134 Guilleminault, C.; Sigwald, J.; Castaigne, P. Sleep Disorders Clinic and Laboratory, Stanford University Medical Center, Stanford, CA 94305 **Sleep studies and therapeutic trial with L-dopa in a case of Stiffman syndrome.** European Neurology (Basel). 10(2):89-96, 1973.

A case of Stiffman syndrome was followed for several years. A trial with L-dopa was performed after diazepam withdrawal. All night polygraphic monitorings of the patient's sleep under diazepam, under no drugs, and under L-dopa were performed. An analysis of sleep stages and electromyographic changes was obtained. A new benzodiazepine (Ro 054023) was tried after L-dopa. A possible imbalance between a catecholaminergic and a GABA-ergic system in the Stiffman syndrome is hypothesized. 19 references. (Author abstract)

171731 Cree, Jean E.; Meyer, Joseph; Hailey, David M. Royal Alexandra Hospital for Sick Children, Brighton BN1 3jN, England **Diazepam in labour: its metabolism and effect on the clinical condition and thermogenesis of the newborn.** British Medical Journal. No. 5887:251-255, 1973.

Following the administration of diazepam to mothers in labor the clinical effects, changes in thermogenesis, and metabolism of the drug in the newborn were observed under carefully controlled conditions. A total maternal dose of 30 mg or less in the 15 hours before delivery had little effect on the infants' state. Larger doses, however, were accompanied by low Apgar scores at birth, apnoecic spells, hypotonia, reluctance to feed, and an impaired metabolic response to a cold stress. Measurement of plasma levels of diazepam and its active metabolite showed that both products were detectable in significant concentrations in some infants for up to 8 days. It is concluded that greater care should be taken in the use of this otherwise effective drug for the treatment of preeclampsia. 16 references. (Author abstract)

171794 Messina, C.; Di Rosa, A. E.; Tomasello, F. Clinica dell Malattie Nervose e Mentali dell' Universita di Messina, Messina, Italy **Habituation of blink reflexes in parkinsonian patients under levodopa and amantadine treatment.** Journal of Neurological Sciences (Amsterdam). 17(2):141-148, 1972.

The habituation of the polysynaptic component of the blink reflexes were studied in 10 Parkinsonian patients treated with levodopa and in nine others who received intravenous amantadine. Under pretreatment conditions all subjects showed a clear-cut defect of habituation of this reflex. Both levodopa and amantadine produced some recovery of habituation, levodopa being more effective than amantadine. Electrophysiological recordings have been compared to clinical phenomena recorded in the same patients under pretreatment conditions and after both drugs were administered. 19 references. (Author abstract)

172271 Glassman, Alexander H.; Hurwic, Maria J.; Perel, James M. Department of Biological Psychiatry, New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Plasma binding of imipramine and clinical outcome.** American Journal of Psychiatry. 130(12):1367-1369, 1973.

The binding of imipramine to plasma protein was examined in 26 depressed patients. In contrast to the findings of previously published reports, the fraction of the drug that remained unbound was found to vary significantly from one patient to another. This finding provides a possible explanation for the discrepancies that have been found in studies that have attempted to correlate plasma levels of antidepressant drugs and clinical outcome. 18 references. (Author abstract)

172972 Bobon, D. P. no address /**The EEG of sleep and psychotropic drugs.**/ EEG de sommeil et psychotropes. Feuillets Psychiatriques de Liege (Liege). 5(2):166-171, 1972.

The effects of different drugs on states of complete wakefulness and paradoxical sleep were studied by means of EEG. Brain centers affected are diagrammed, and experiments conducted with cats are cited. Human EEGs are also considered. The use of certain drugs for specific sleep problems is described. Caution is recommended in the use of any drug prescribed for sleep problems because of the differences of opinion expressed to date as to the neurohumoral control of sleep.

173056 Sarbin, Theodore R. Stevenson College, University of California, Santa Cruz, CA 95064 **On the recently reported physiological and pharmacological reality of the hypnotic state.** Psychological Record. 23(4):505-511, 1973.

A recent study by Ulett, Akpinar, and Itil that explored the reality of a hypnotic state is critically examined. It is suggested that electroencephalograph profiles and response to psychotrop-

ic drugs, contrary to the claims of the investigators, provide no warrant for the conclusion that a special mental state has been isolated, identified, or demonstrated. 20 references. (Author abstract)

174347 Hollister, Leo E. Veterans Administration Hosptial, Palo Alto, CA **Interactions in man of delta-9-tetrahydrocannabinol: I. alphamethylparatyrosine.** Clinical Pharmacology and Therapeutics. 15(1):18-21, 1974.

The interaction of alphamethylparatyrosine (AMPT) and delta-9-tetra-hydrocannabinol (THC) was studied in three separate experiments, two giving THC orally to six and four male subjects, respectively, and one administering it to six male subjects, intravenously. Pretreatment with doses of 2.0to 4.0gm of AMPT was found to produce no major qualitative or quantitative change in the effects of THC. Some accentuation of the totall intensity of THC was apparent in each experiment, but it was not ascertainable whether this difference was due to additive pharmacologic effects or diminished catecholamine concentrations in the brain. It is concluded that mental effects of THC are not mediated primarily through catecholamines, but rather by the balance between the concentrations of these amines and others, such as acetylcholine or serotonin. 11 references. (Author abstract modified)

174473 Nutt, J. G.; Jasinski, D. R. NIMH Addiction Research Center, Lexington, KY 40507 **Diuretic activity of a new narcotic antagonist in man (Bristol compound 2605). (Unpublished paper).** Lexington, Ky., NIMH Addiction Research Center, 1973. 1 p.

During the clinical evaluation of the narcotic antagonist l-N-cyclopropylmethyl-3,14-dihydroxymorphinan (l-BC-2605) as a potential agent for treatment of narcotic addiction, Ss reported polyuria. This phenomenon was evaluated during a double-blind, crossover comparison in 10 subjects of the subjective effects of s.c. placebo, 0.5and 1.0mg of cyclazocine and 2.0and 4.0mg of 1-BC-2605 by monitoring subjects' fluid intake and urine output. Both 1-BC-2605 and cyclazocine significantly increased urine output without affecting fluid intake. In 8 water deprived Ss, 1.0to 4.0mg of 1-BC-2605 s.c. quadrupled 6 hour urine output and decreased urine osmolality, often to below serum osmolality, but produced no significant alteration in creatinine clearance, solute excretion, electrolyte excretion or blood pressure. 10mg of naloxone s.c. had no diuretic effect in 3 water deprived subjects and did not antagonize the diuretic effect of 1-BC-2605. Results suggest that the diuretic affect is an agonistic action of 1-BC-2605 produced by inhibition of ADH release. (Author abstract modified)

174505 Ikuta, Takumi. Department of Neuropsychiatry, Faculty of Medicine, Kyushu University, Japan **Re-investigation on the effects of thiopental on the human somatosensory evoked response.** Fukuoka Acta Medica (Fukuoka). 64(7):276-283, 1973.

The effect of thiopental on the human SER (Somatosensory Evoked Response) is reinvestigated by adopting Inter-Personal Averaging (IPA) in order to obtain IPA-SER patterns, and the changes of the pattern due to the drug were studied in schizophrenics. Further, an attempt was made to find out by which indicator the changes of IPA-SER patterns were most correctly measured. The IPA-SER patterns before thiopental injection consisted of the major positive peak followed by a major negative peak. The major positive peak was depressed to become hollow after thiopental injection. It is concluded that Sum(1), which had been developed completely separate from the peak to peak measurement as an indicator for pattern recognition, was a better indicator for expressing the change of SER due to thiopental than the latencies and the amplitude which belong to the peak to peak measurement. 33 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

167711 Levine, Jerome; Lipman, Ronald S. NIMH, 5600 Fishers Lane, Rockville, MD 20852 **Psychotherapeutic drug trials among English general practitioners.** In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 79-84).

Psychotherapeutic drug trials carried out by 400 general practitioners in Great Britain, with the objective of evaluating the drugs are discussed. Several drugs used in treating anxiety and neurotic depression are discussed. It is concluded that there are many advantages in doing research work in the general practice setting; it is recommended that support for the General Practitioner Research Group in England be continued.

167712 Lehmann, Heinz E.; Ban, Thomas A. Dept. of Psychiatry, McGill U., Montreal, Quebec, Canada **Megavitamin treatment, culture**

and tranquilizers, drugs for the aged: projects of a Canadian grant. In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 85-93).

The efficacy of drugs for mental disorders is assessed. Megavitamin therapy in the treatment of schizophrenia is analyzed. Transcultural studies with antidepressant tranquilizing drugs are also researched. Finally, therapeutic response in psychogeriatrics is predicted. 5 references.

167921 Nakazawa, Yoichi; Tachibana, Hisayuki; Kotorii, Makoto; Ogata, Masamichi. Department of Neuropsychiatry, School of Medicine, Kurume University, Kurume, Japan **Effects of L-DOPA on natural night sleep and on rebound of REM sleep.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 27(3):223-230, 1973.

The relationship between rapid eye movement (REM) sleep and the central catecholamines in man was investigated by administering L-DOPA. No effect was found on the natural night sleep. The rebound elevation of REM sleep in the recovery night after partial differential REM sleep deprivation was affected by the dose on both recovery nights. The central noradrenaline seems to be more easily and readily synthesized from exogenous L-DOPA in the recovery night sleep than in natural night sleep. The rebound elevation of REM sleep disappears as a consequence of rapid restoration of the central noradrenaline. Therefore these results seem to be one of the reasons for REM in man. 18 references. (Author abstract)

168419 Zung, William W. K. Duke University Medical Center, Durham, NC **The effect of placebo and drugs on human sleep.** Biological Psychiatry, 6(1):89-92, 1973.

The effect of placebo and hypnotic drugs on human sleep was investigated in men and women between 20 and 45 years of age. Drugs were triclofos and phenobarbital. Continuous recordings of the EEG, electrooculogram, and electromyogram were used to measure sleep, rapid eye movement (REM) and muscle potentials of all Ss. The all night tracings were visually scored for stages of sleep REM using a standardized system. Results indicated that there is a placebo effect during sleep and REM states at night, but must be looked at as preliminary taking into account the small number of Ss and the few nights under which each condition was investigated. 3 references.

168523 Prechtl, H. F. R.; Theorell, K.; Blair, A. W. Dept. of Developmental Neurology, University of Groningen, The Netherlands **Behavioural state cycles in abnormal infants.** Developmental Medicine and Child Neurology (Tadworth, Surrey, England). 15(5):606-615, 1973.

Polygraphic methods were used to evaluate the percentage distribution of sleep and awake states and the mean duration of individual periods spent in these states in infants with Down's syndrome, bilirubinemia and in a heterogeneous group of high risk infants. Not unexpectedly, alterations from previously established normal values were found, as were differences in pattern between the groups. Infants with Down's syndrome spend more time awake at the expense of time in state 2 (active sleep), but prolonged sleep cycles are occasionally possible. Bilirubinemic infants showed a drastic reduction in the amount of time spent in the awake states. Individual periods spent in state 2 were significantly longer, producing also a prolonged sleep cycle duration. The high risk group spent abnormally short periods in state 2 and none of the infants studied produced a long sleep cycle. The amount of time spent in awake states varied widely. Antiepileptic drugs induced more and longer individual periods of state 1 (quiet sleep) at the expense of state 2. The pathophysiological mechanisms behind these alterations in the state cycle are discussed. 9 references. (Author abstract)

168831 Bond, Alyson J.; Lader, Malcolm H. Dept. of Psychiatry, Institute of Psychiatry, De Crespigny Park, London, S.E.5, England **The residual effects of flurazepam.** Psychopharmacologia (Berlin). 32(3):223-235, 1973.

The residual effects of flurazepam were investigated. Eight normal Ss were tested on a large battery of physiological and psychological tests 12, 15 and 18h after a hypnotic dose of butobarbitone sodium, flurazepam or a placebo. Ss received all four treatments in a balanced design. Tests included self-ratings of mood, the EEG, the auditory electroencephalographic evoked response, reaction time, the digit symbol substitution test and the symbol copying test. Both drugs were hypnotics according to the ratings but they also influenced mood the following day. The EEG and the evoked response showed significant changes up to 18 h after both drugs. The psychological tests were only affected 12 h after the drugs. 18 references. (Author abstract)

168901 James, Basil; James, Norman McI. University of Otago Medical School, Dunedin, New Zealand **Tranquilizers and examination stress.** Journal of the American College Health Association. 21(3):241-243, 1973.

The value of the anxiolytic drugs chlordiazepoxide and haloperidol, and of placebos in relieving examination anxiety was investigated, in a double blind cross-over technique using 144 university students. Subjects were not under psychiatric treatment for emotional disorders and were considered representative of the student population. The Ss performed the Digit Symbol Translation test under test conditions designed to evoke an anxiety response, and each subject was tested four times at weekly intervals with different symbols for each test. Changes in translation ability, anxiety levels, and pulserates were recorded and the Ss' reactions to the drugs administered before the tests was analyzed. The effects of anxiety seemed to diminish with experience but were not influenced by the drugs. Placebos were as effective in improving test performance as haloperidol in small doses. The comparatively poorer performance of Ss on chlordiazepoxide may be related to a sedative effect in that drug. 5 references. (Author abstract modified)

168976 Eliseo, M.; Ales, M. Istituti Ospedalieri Riuniti 'Pietro Pisani', Ospedale Psichiatrico, Palermo, Italy **/Psychopathological importance and therapeutic effects of a combination of Hydergin and thioridazine in psychiatric syndromes in the aging./** Rilievi psicopatologici ed effetti terapeutici dell'associazione hydergina-tioridazina nelle sindromi psichiatriche dell'eta involutiva. Pisani (Palermo). 94(1-3):243-263, 1970.

Results of testing a product that is a combination of Hydergin and thioridazine on 88 men and women patients between 60 and 75 years of age are discussed. Forty six (25 men, 21 women) were hospitalized, 42 (23 men, 19 women) were outpatients. Results are tabulated and the mathematics involved in reaching statistical determinations are detailed. No significant differences in therapeutic results were found in the two groups. 78 references.

169085 Patch, Vernon D. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **Marihuana use in man: an experimental inquiry -- clinical psychiatric impressions.** Psychopharmacology Bulletin. 9(4):52-54, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, 10 casual and 10 heavy marihuana smokers were studied to determine the marihuana consumption patterns of the two groups under free choice conditions. Assessments included evaluations of mood states, group and individual behavior patterns, psychomotor skills, physiological functions, free choice and work contingent on operant acquisition marihuana consumption patterns, and clinical psychiatric evaluations. Subjects' assessments of the quality and effects of the marihuana they had consumed during the study provide some suggestive evidence for the development of tolerance to the effects of marihuana. (Journal abstract modified)

169086 Salzman, Carl; Kochansky, Gerald E.; Porrino, Linda J. Psychopharmacology Research Lab., Harvard Medical School at the Massachusetts Mental Health Center, Boston, MA **The effect of marijuana on hostility in an experimental group setting: preliminary observations.** Psychopharmacology Bulletin. 9(4):54-55, 1973.

In a paper presented at the Eleventh Annual Meeting of the American College of Neuropsychopharmacology, the effect of marihuana on hostility in a group setting was measured by: assessment of verbal interpersonal hostility; assessment of hostile inner-states; and interpersonal perception of hostility. Subjects who smoked marihuana and then interacted in a group perceived themselves and their group colleagues as less hostile and more friendly. However, nonintoxicated and experimenter observers rated the subjects as manifesting a shift in style of hostile communication from overt to indirect rather than showing any readily apparent quantitative change. In particular, there was a dramatic increase in the use of sarcasm to express hostility. (Journal abstract modified)

169457 Serrano, Alberto C.; Forbis, Orie L., Jr. Department of Psychiatry, University of Texas Medical School at San Antonio, San Antonio, TX **Haloperidol for psychiatric disorders in children.** Diseases of the Nervous System. 34(5):226-231, 1973.

During a double-blind study, children, 6 to 12 years old, with severe behavior problems were treated with either haloperidol or fluphenazine. They were seen at a community mental health clinic for outpatients over a 12 to 14 week period. Significantly more patients treated with

haloperidol showed global improvement at the end of the study. Haloperidol had a faster onset of action and alleviated symptoms in the affect and social behavior clusters in significantly more patients than did fluphenazine, whereas both drugs had similar effects on symptoms in the motor behavior cluster. Haloperidol seemed to be particularly beneficial in children whose conditions were deteriorating despite therapy with other psychotropic drugs. 10 references. (Author abstract)

169462 Jauch, Thomas E.; Loch, Jerry; Earl, Joseph; Bauer, William. Northwest Human Resources Center, Ltd., Rolling Meadows, IL **Droperidol -- a preferred neuroleptic in narcoanalysis.** Diseases of the Nervous System. 34(5):259-262, 1973.

The use of Droperidol (a butyrophenone derivative) as a narcoanalytic agent is discussed. When administered in selected cases to facilitate the treatment of resistive patients, it was found that the patient could resume his activities soon after the interview was finished. The drug produced the following effects: narcolepsy; stable EEG; amphetamine antagonism; central and autonomic nervous system sedative action; mild thymic excitation; and inhibition of aberrant responses which lessened the possibility of uncovering psychotic processes. The treatment of delinquent adolescents with Droperidol analyses is considered. A case history and sample analysis are presented. 6 references.

169745 James, B.; James, N. McI. Department of Psychological Medicine, University of Otago Medical School, Dunedin, New Zealand **Low dosage haloperidol and induced anxiety in normal volunteers.** New Zealand Medical Journal (Dunedin, New Zealand). 78(498):210-212, 1973.

A double-blind cross-over trial using normal paid volunteers to measure the effect of low dosage haloperidol upon induced anxiety is described. No significant effect was found upon either subjective anxiety or pulse rate measurements. Ss on haloperidol or placebo performed better in the test situation and reported fewer sedative side-effects than those on chlordiazepoxide. 10 references.

171241 Jasinski, D. R.; Griffith, J. D.; Carr, C. B. NIDA Addiction Research Center, Box 2000, Lexington, KY 40507 **Abuse potential of etorphine (M99) I. subjective effects and physical dependence. (Unpublished paper).** Lexington, KY, NIMH, 1973. 1 p.

The abuse potential of etorphine (M99), a morphine like agent estimated 500 to 1000 times more potent and used for game immobilization, was studied in human Ss. To assess subjective effects, euphoria and miosis, doses of 25, 50, and 100 micrograms were used, and morphine (15 and 30mg) and placebo were given s.c. at weekly intervals to 12 Ss. Opiate effects were found, since M99 was identified as an opiate by Ss and observers, produced miosis, and increased scores on scales measuring opiate like subjective effects and euphoria. Effects were apparent within 5 min, maximum at 1/2 hr and decreased rapidly to placebo level within 3 to 4 hr. M99 was 500 to 1000 times more potent than morphine in producing subjective effects and miosis. Hourly abstinence observations indicated M99 suppressed morphine abstinence, but only for 1 to 2 hr. Subsequently complete suppression of abstinence was obtained with M99, 50 micrograms/70kg administered s.c. every 2 hr and then hourly for a total dose of 600 micrograms/70kg M99. It is concluded that M99 is a very potent, short acting, morphine like drug in man, with a rapid onset of action and a high abuse potential. (Author abstract modified)

171299 Downing, Robert W.; Rickels, Karl; Dreesmann, Helmut. Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Orthogonal factors vs. interdependent variables as predictors of drug treatment response in anxious outpatients.** Psychopharmacologia (Berlin). 32(2):93-111, 1973.

Two forms of multiple regression analysis, one based upon a set of individual variables, one based upon a set of orthogonal factors generated from them, were used to predict response to treatment in a group of 199 primarily anxious, neurotic outpatients treated for a 4 week period with either diazepam or phenobarbital. Greater improvement was found in patients who: 1) enjoyed greater social and personal advantage; 2) participated in a more empathetic treatment relationship; 3) were oriented toward drugs and away from psychotherapy as a primary treatment modality; 4) had less severe presenting symptomatology; and 5) had sufficient cognitive differentiation to realize that their problems were emotional in origin. Diazepam was superior to phenobarbital in employed patients and in patients with more severe somatizing tendencies, while the

relative effectiveness of the two medications was reversed in unemployed patients and those with limited somatizing tendencies. 28 references. (Author abstract)

173516 Stillman, Richard C.; Galanter, M.; Lemberger, L.; Fox, S.; Weingartner, H.; Wyatt, R. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **THC: metabolism and subjective effects of stress. (Unpublished paper).** Washington, DC, NIMH, 1973, 1 p.

The relationship between affective, cognitive, physiological, and metabolic parameters of marihuana smoking was investigated. In the stress condition (repeated venipuncture) there was a more rapidly declining 'high' reported by subjects on a 0-10 scale despite early attainment of approximately equal highs under the stress - nonstress conditions. In the stress condition also, mean pulse rate increases induced by THC were significantly lower than under nonstress conditions; mean pulse started higher but peaked lower in the stress condition. Eleven test items differed significantly between the stress and nonstress conditions, of which only half were obviously related to the noxious stimuli of the stress condition. The others seem to refer to qualities of being intoxicated which are separate from the euphoria - dysphoria dimension. These data document the anecdotal report of stress bringing one down from a marihuana high. Additional experiments suggest that the same effect can be produced by instituting a period of difficult mental activity.

173521 Kaplan, Jonathan; Dawson, Susan; Vaughan, Thomas; Wyatt, Richard. Laboratory of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Sleep: a tool to study chlorpromazine's action. (Unpublished paper).** Washington, DC, NIMH, 1973, 1 p.

Sleep was used as a tool to investigate the mechanisms behind the antipsychotic effects of chlorpromazine (CPZ). Ss had been hospitalized from 1 to 15 years with a diagnosis of chronic schizophrenia. It was found that when compared to placebo, CPZ was a potent sedative. Sleep latency, time spent awake, and actual sleep time was significantly increased. Stage II, delta sleep, and nonrapid eye movement (REM) sleep time was increased. It was therefore demonstrated that prolonged CPZ administration is associated with an increase in slow wave sleep. The effect of CPZ on REM sleep was also impressive. There was a significant increase in REM activity and REM density. REM latency was significantly increased. The amount of REM sleep time and the percentage REM of actual sleep time were not significantly changed. (Author abstract modified)

174041 Cousens, Kenneth; DiMascio, Alberto. Boston State Hospital, 591 Morton Street, Boston, MA 02124 **(-)delta9 THC as an hypnotic: an experimental study of three dose levels.** Psychopharmacologia (Berlin). 33(4):355-364, 1973.

(-)delta9-THC was found to significantly decrease the time it takes to fall asleep in physically healthy insomniacs. Once asleep, interruptions of sleep were not significantly altered over the whole night. The (-)delta9-THC tended to be associated with some decrease in awakenings in the first half of the night. The primary side-effect experienced by the subjects at all dose levels in the Presleep phase was temporal disorganization and mood alterations. There was an increase in intensity of side-effects and number of subjects affected with increasing dosage. The most significant side-effect was a hangover phenomenon, or continued high the next day, with some residual of temporal disorganization. It increased in intensity and duration with increase in dosage. 10 references. (Author abstract modified)

174043 Dittrich, A.; Battig, K.; von Zepplin, Ilka. Psychiatrische Universitatsklinik, Burgholzli, Forschungsdirektion, Postfach, CH-8029, Zurich, Schweiz **Effects of (-)delta9-trans-tetrahydrocannabinol (delta9-THC) on memory, attention and subjective state: a double blind study.** Psychopharmacologia (Berlin). 33(4):369-376, 1973.

In a double-blind study, cross over design, on 37 volunteers, several effects of an orally administered dosage of 15 mgs (-)delta9-trans-tetrahydrocannabinol (delta9-THC) were assessed. The results did bear out the hypotheses that the impairment of attention and information storage in the long-term memory as well as depersonalization and temporal disintegration phenomena induced by delta9-THC are interrelated. The sequence of information retrieval from memory was found to be changed by delta9-THC. 14 references. (Author abstract)

174132 Reilly, E.; Halmi, Katherine A.; Noyes, R., Jr. Department of Psychiatry, University of Iowa, College of Medicine, Iowa City, IA Elec-

troencephalographic responses to lithium. International Pharmacopsychiatry (Basel). 8(4):208-213, 1973.

Electroencephalographic changes were studied in 12 healthy subjects given lithium carbonate. Findings indicate that although half demonstrate EEG abnormalities, all represented accentuations of previous EEG variations. It is concluded that while EEG abnormalities may occur during lithium administration, they more frequently represent accentuations of previous abnormalities than they do specific drug effects upon the normal EEG. (Author abstract modified)

174210 Hurst, Paul M.; Weidner, Marrianna F.; Radlow, Robert: Ross, Sherman. Institute for Research, 257 S. Pugh St., State College, PA 16801 **Drugs and placebos: drug guessing by normal volunteers.** Psychological Reports. 33(3):683-694, 1973.

How well college student Ss could distinguish some common psychoactive drugs in terms of four gross categories: stimulant; depressant; tranquilizer; and no effect was determined. After drug ingestion, a series of experimental tasks, differing among the experiments, were used. At the end of each session, S reported on drug effects and classified each drug into a category. In one experiment only the first two categories were used. Differences in drugs received accounted for only a small part of the variance in assigned categories. Amphetamines at the dose levels used were better discriminated from placebo than were other drugs. Limited prior experience in being a S in drug experiments may facilitate drug recognition. This possibility was discussed. 12 references. (Author abstract modified)

174348 Whitsett, Thomas L.; Hoyt, Harvey J.; Czerwinski, Anthony W.; Clark, Mervin L. Oklahoma City VA Hospital, Room A-716, 921 N.E. Thirteenth St., Okalhoma City, OK 73104 **Effects of mebutamate on the electroencephalographic sleep profile.** Clinical Pharmacology and Therapeutics. 15(1):51-58, 1974.

The initial and short-term cumulative effect of mebutamate on the various stages of sleep were studied. The effect of mebutamate on the electroenephalographic sleep profile in ten healthy, noninsomniac normal males was evaluated. Placebo was administered on nights 1 to 4, mebutamate on nights 5 to 7, and placebo on nights 8 and 9. The results demonstrate that mebutamate significantly altered the electroencephalographic sleep profile. REM sleep was significantly depressed but was not associated with rebound; a low amplitude, high frequency beta rhythm emerged. A significant increase in stages two and four sleep patterns was found, the latter in the 100 % range. 22 references. (Author abstract modified)

174479 Jasinski, Donald R.; Nutt, J. G.; Bunney, W. E. NIMH Addiction Research Center, P.O. Box 2000, Lexington, KY 40507 **Lithium (Li): lack of effect on morphine (MS) euphoria. (Unpublished paper).** Lexington, Ky., NIMH Addiction Research Center, 1973. 1 p.

Studies were conducted to determine if Lithium (Li) would alter the subjective state produced by morphine (MS). Li alone produced mild dysphoria, nausea, and sleepiness. At 5 day intervals between the 10th and 20th days of Li, each subject received 15mg MS, placebo, and 7.5mg of MS. MS effects were measured with changes in pupil diameter, scores on opiate sign and symptom scales, liking scales, and items from the Morphine-Benzedrine Group scale. The MS effects during Li were compared with similarly measured effects of placebo and 15mg MS administered prior to Li, and 7.5and 15mg of MS administered 4 to 6 weeks after discontinuing Li. Comparison of scale scores and miosis for corresponding drug treatments on and off Li indicated no significant differences, and it was concluded that Li had no effect on miosis or subjective state produced by MS. (Author abstract modified)

174609 Meltzer, H. Y.; Stahl, S. M. University of Chicago Pritzker School of Medicine, 950 East 59th Street, Chicago, IL 60637 **Platelet monoamine oxidase activity and substrate preferences in schizophrenic patients.** Research Communications in Chemical Pathology and Pharmacology. 7(2):419-431, 1974.

Blood platelet monoamine oxidose (MAO) activity was measured in 12 chronic schizophrenic (CS) and 10 acute schizophrenic (AS) patients, and in 15 normal controls using four substrates. Platelet MAO activity of the CS patients was significantly lower than that of controls with all four substrates. With the AS patients, platelet MAO activity was lower than that of the controls only with meta-iodobenzylamine (MIB) or tyramine as substrates. Octopamine tended to be the best substrate for both patient groups and the lowest for the control group. MIB was the best substitute in

distinguishing the schizophrenic patients and controls. Variations in the affinities of MAO for the multiple substrates suggest that the platelet MAO of AS and CS patients, and controls may contain different forms of MAO. 31 references. (Author abstract)

15 TOXICOLOGY AND SIDE EFFECTS

167572 De Silva, K. L.; Muller, P. J.; Pearce, John. Combined Neurological Service, Hull Royal Infirmary, Hull, England **Acute drug-induced extrapyramidal syndromes.** Practitioner. 211(1263):316-320, 1973.

Ten cases of acute drug induced extrapyramidal syndromes seen in a single neurological unit over a 2 year period are reported. In five cases the offending drug was a phenothiazine of the piperazine group, while in four cases it was metoclopramide. Findings indicate that all reactions occurred shortly after treatment was started and that all cases were referred without a specific diagnosis. The fact that all patients recovered within hours of discontinuing the offending drug and instituting therapy with an anticholinergic drug or with diazepam is discussed. It is suggested that there is a need for greater awareness of this condition, thus saving unnecessary investigations and therapy in such patients. 10 references. (Author abstract modified)

167587 Jus, K.; Jus, A.; Villeneuve, A.; Villeneuve, R. Research Division, Hopital St. Michael-Archange, Quebec, Canada **Influence of concentration and motor performance on tardive dyskinesia and rabbit syndrome.** Canadian Psychiatric Association Journal (Ottawa). 18(4):327-330, 1973.

A polygraphic study of the influence of concentration and motor performance on certain extrapyramidal movements induced by neuroleptics, such as tardive dyskinesia and rabbit syndrome, in 29 schizophrenic patients is reported. It is concluded that the use of polygraphic techniques in patients with tardive dyskinesia constitutes a useful tool for investigating quantitative and qualitative changes in these abnormal involuntary movements. Other findings are presented. 12 references.

167832 Naditch, Murray P. Cornell University, Ithaca, NY **Acute adverse reactions to psychoactive drugs, drug usage, and personality. (Unpublished paper).** Ithaca, NY, Cornell University, 1973. 42 p.

Operational measures of acute adverse reactions to psychoactive drugs were developed, and some preliminary hypotheses concerning relationships among three personality constructs, drug use and acute adverse reactions were tested. Data were consistent with a causal model in which locus of control influenced acute adverse reactions directly and indirectly through its effects in increased usage of lysergic acid diethylamide (LSD) and increased hypochondriasis. Relative discontent influenced adverse reactions indirectly through interaction with locus of control and increased hypochondriasis. Hypochondriasis and LSD usage directly effected acute adverse reactions. Drug usage and acute reactions were increased when drug usage was motivated by solution of personal problems. LSD usage directly effected acute adverse reactions after partialling out the problem-solving motive, but marihuana usage did not. 57 references. (Author abstract modified)

168319 Ananth, J. V.; Jain, R. C. St. Mary's Hospital, 3830 Lacombe, Montreal, Quebec, Canada **Benztropine psychosis.** Canadian Psychiatric Association Journal (Canada). 18(5):409-414, 1973.

Twelve cases of toxic psychosis in psychiatric patients receiving benztropine for the treatment of drug - induced extrapyramidal signs are reviewed, the significance of such reactions explored, and remedial measures suggested. Patients of all age groups are susceptible to this reaction, and patients of both sexes are affected. All 12 patients were on therapeutic doses of benztropine. The average duration of administration of the drug before the occurrence of psychosis was 7.5days. Toxic psychosis is very anxiety provoking to the patient and the relatives, in addition to posing diagnostic and therapeutic riddles to the psychiatrist. Careful prescription of the drug prevents many adverse reactions. 13 references.

168505 Herrero, Fernando A. 4500 S Lancaster Rd, Dallas, TX 75216 **Lithium carbonate toxicity.** Journal of the American Medical Association. 226(9):1109-1111, 1973.

A case history of lithium carbonate toxicity in a 59-year-old man receiving the drug as treatment for manic depressive psychosis is discussed. Lithium carbonate therapy, uncomplicated by other factors, can give rise to a deep coma even if the serum levels of lithium are within the desired range. The patient had been treated with the drug for less than 1 year and developed progressive im-

pairment of consciousness. A few days after the medication was discontinued, a slow but complete recovery resulted. Lithium accumulation in the brain is postulated. 8 references. (Author abstract modified)

168526 Mowat, Alex P. Dept. of Child Health, King's College Hospital Medical School, Denmark Hill, London, SE5 8RX, England **Dystonic reactions to drugs.** Developmental Medicine and Child Neurology (Tadworth, Surrey, England). 15(5):654-655, 1973.

Dystonic reactions to drugs in children are discussed. Parkinsonism, akathisia, and acute dystonia are the three main syndromes of disturbed extrapyramidal function induced by drugs, particularly the major tranquillizers. Current evidence suggests that the mode of action of these drugs in producing extrapyramidal side effects involves derangement of dopamine (DA) metabolism. It is apparent that normal DA metabolism in the striatum is critical both for normal motor activity and for stereotyped movements of extrapyramidal origin, and its derangement is associated with a definite disturbance of the extrapyramidal control of motor function. Further studies are needed in drug metabolism and its variation from individual to individual and in different parts of the brain. The elucidation of the function of the complex striatal system, with a greater understanding of the effect of age on these aspects of drug metabolism will be necessary to explain fully the iatrogenic extrapyramidal syndromes. 6 references.

168619 Maskin, Michael B.; Riklan, Manuel; Chabot, David. Dept. of Psychology, California State College, San Bernardino, CA 92407 **Emotional functions in short-term vs. long-term L-Dopa therapy in Parkinsonism.** Journal of Clinical Psychology. 29(4):493-495, 1973.

Emotional aspects of short and long term L-Dopa therapy used in the treatment of Parkinsonism are discussed. Forty five subjects were divided into three equal groups. Two random groups were subjected to short and long-term L-Dopa treatments while the last group was comprised of normal hospital employees. MMPI and two other personality tests were administered to the subjects. The results seem to substantiate the belief that the initial psychological improvement, particularly in depression, of the patient as a result of short-term L-Dopa treatment does not continue after a period of 2 years. A subtle deteriorating in psychological functioning appears to begin at this time as a result of chemical toxicity in altered brain catecholamine states, and insight and realization that L-Dopa therapy can only offer limited help in the course of a progressive degenerative disease. 7 references. (Author abstract modified)

169140 Kiloh, L. G.; Smith, J. Sydney; Williams, S. E. School of Psychiatry, Univ. of New South Wales, Little Bay, New South Wales, Australia **Antiparkison drugs as causal agents in tardive dyskinesia.** Medical Journal of Australia (Sydney). 2(12):591-593, 1973.

The cases of three patients in whom a phenothiazine induced tardive dyskinesia was aggravated by benztropine are described. It is suggested that in some cases antiparkinson drugs may have a significant adjuvant effect in provoking tardive dyskinesia. 17 references. (Author abstract)

169376 Chase, Thomas N.; Holden, E. Michael; Brody, Jacob A. Neurology Unit, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Levodopa-induced dyskinesias: comparison in parkinsonism-dementia and amyotrophic lateral sclerosis.** Archives of Neurology. 29(5):328-330, 1973.

The incidence of levodopa induced dyskinesias in 20 Guamanian patients with parkinsonism dementia (PD) was compared with that found in 14 Guamanians with amyotrophic lateral sclerosis (ALS), who were matched for dose and duration of drug exposure. While 55% of the PD patients developed abnormal involuntary movements during the first 6 months of treatment, none of the ALS patients manifested this complication. In PD patients no definite corrleation could be documented between pretreatment parkinsonian severity or response to levodopa and the appearance of dyskinesias. The results suggest that lesions of the type which produce Parkinson disease increase the susceptibility to levodopa induced dyskinesias, but that denervation supersensitivity alone does not account for this phenomenon. 29 references. (Author abstract)

169486 Levy, Steven T.; Forrest, John N., Jr.; Heninger, George R. Adult Psychiatry Branch, Psychiatric Assessment Section, NIMH, Building 10, NIH, 9000 Rockville Pike, Bethesda, MD 20014 **Lithium-induced diabetes insipidus: manic symptoms, brain and electrolyte correlates, and chlorothiazide treatment.** American Journal of Psychiatry. 130(9):1014-1018, 1973.

A patient with lithium induced, vasopressin insensitive diabetes insipidus was studied during two consecutive manic episodes that were successfully treated with lithium. Polyuria occurred several days after lithium induced brain electrical changes were observed, and at serum lithium concentrations close to 1.0mEq/liter. Polyuria began during a period of behavioral improvement and persisted after the manic symptoms subsided. Polyuria did not occur in association with serum lithium concentrations over 1.8mEq/liter, and a fourfold increase in sodium intake did not reduce the polyuria. Chlorothiazide reduced polyuria and permitted the patient to continue the lithium treatment. 19 references. (Author abstract)

169492 Rifkin, Arthur; Kurtin, Stephen B.; Quitkin, Frederic; Klein, Donald F. Aftercare Clinic, Hillside Division, Long Island Jewish-Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004 **Lithium-induced folliculitis.** American Journal of Psychiatry. 130(9):1018-1019, 1973.

Twelve patients receiving long-term treatment with lithium who developed folliculitis on their extremities and/or trunks were examined. The rash disappeared in three patients who discontinued lithium therapy, and in one patient it reappeared when she again received lithium. It is concluded that folliculitis is a common, but not serious, side-effect of lithium treatment. 6 references. (Author abstract modified)

169635 Schubert, Daniel S. P. Dept. of Psychiatry, Case Western Reserve University, School of Medicine, Cleveland, OH **The effect of lithium and other antidepressant medications on the autonomic nervous system.** Current Therapeutic Research. 15(11):862-865, 1973.

Saliva output, body temperature, heartrate, and blood pressure were measured in depressed patients undergoing antidepressant medication treatments. After a preliminary period without medications, various drug treatments were given, but without producing regular mood changes. It was discovered that lithium produced an elevation in body temperature and saliva output in the depressed women subjects. The saliva output returned to prelithium levels after 2 to 3 weeks, but the body temperature remained elevated throughout the observation period of 4 to 5 weeks. Suggested stimuli causing the temperature rise and saliva output are offered. Effects of other medications which produced decreased saliva output are noted. No regular changes in blood pressure or heartrate were observed as a result of lithium. 10 references.

169869 Baer, Leslie; Glassman, Alexander H.; Kassir, Suham. 722 W 168th Str., New York, NY 10032 **Negative sodium balance in lithium carbonate toxicity: evidence of mineralocorticoid blockade.** Archives of General Psychiatry. 29(6):823-227, 1973.

The mechanisms leading to development of lithium carbonate toxicity in patients maintained on a constant sodium and fluid intake and its recognition are discussed. Intoxication by lithium carbonate and its associated symptoms are described. Two manic-depressive patients were mainntained on a constant sodium and fluid intake. Experimental rats also exhibited negative sodium balance and lithium toxicity. The renal response to deoxycorticosterone acetate (DOC) was evaluated in groups of control and lithium carbonate rats. A blunted response to the sodium retaining properties of DOC was observed. It is concluded that these observations demonstrate a pathogenic cycle in lithium carbonate toxicity. Mineralocorticoid blockade induced by already toxic concentrations of lithium carbonate promotes renal sodium wasting which leads to further lithium retention and increased toxicity. Blockade of sodium transport in other organ systems is also considered. 16 references. (Journal abstract modified)

171275 Aritome, Teruchika. Tochigi Prefectual Okamotodai Hospital, Japan **An autopsy case of schizophrenia complicated with Parkinsonism induced by perphenazine.** Kyushu Neuro-psychiatry (Fukuoka). 19(1):58-63, 1973.

An autopsy of a case of schizophrenia complicated with Parkinsonism induced by perphenazine is discussed. The patient, a 33-year-old male, had been diagnosed schizophrenic at 18 years of age. Since 30 years of age, the patient had been treated with chlorpromazine, 16.65g per day. At age 33, the dose was increased to 21.65g concurrently with perphenazine (32mg/day), promethazine(100mg/day) and trihexyphenidyl(2mg/day) for all days. Perphenazine was terminated due to parkinsonian side-effects, while other drugs were continued. The patient died on day 3. The autopsy revealed extensive brain cell damage and cell disappearance with a pattern differing from paralysis agitans and postencephalitic parkinsonism. 21 references. (Author abstract modified)

171296 Kurioka, Yoshiyuki; Taniwa, Mitsuhiko. Hanna Sanatorium, Japan **The electrocardiographic abnormality induced by chlorpromazine.** Clinical Psychiatry (Tokyo). 14(9):797-805, 1972.

Electrocardiographic abnormalities induced in schizophrenic patients treated with chlorpromazine were studied. Examples of extrasystole, tachycardia, bradycardia and auricular fibrillation are described. Causes of these abnormalities are not clear. 33 references.

171506 VanPutten, Theodore; Mutalipassi, Louis R.; Malkin, Michael D. Brentwood VA Hospital, Wilshire & Sawtelle Blvd., Ward 210-C, Los Angeles, CA 90072 **Phenothiazine-induced decompensation.** Archives of General Psychiatry. 30(1):102-105, 1974.

Adverse mental reactions to phenothiazines were evaluated in a systematic study of 80 patients diagnosed schizophrenic and receiving phenothiazines in conventional dosages. Nine patients experienced dramatic exacerbations of psychosis on phenothiazines with a piperazine side group -- particularly fluphenazine enanthate. These exacerbations of psychosis are associated with a subtle akathisia. Exacerbations of psychosis were promptly reversed by biperiden (Akineton) -- an anticholinergic drug, given intramuscularly. It is proposed that extrapyramidal involvement can have a prominent mental component which resembles an exacerbation of schizophrenia. 26 references. (Author abstract)

171974 Crane, George E. Research Department, Spring Grove State Hospital, Baltimore, MD 21228 **Pseudoparkinsonism and tardive dyskinesia.** Archives of Neurology. 27(5):426-430, 1972.

The hypothesis that tardive dyskinesia is more likely to develop in patients with pseudoparkinsonian symptoms than in patients not exhibiting such manifestations was tested. The hypothesis was supported by: 1) observation of neurological changes in 55 schizophrenic patients taken off a regimen of neuroleptic drugs; 2) a study of the evolution of symptoms in 400 subjects on various drug regimens over a 1 year period; and 3) a controlled investigation of the effects of gradual removal of neuroleptics in four samples of patients exhibiting a variety of drug induced side-effects or no drug related neurological manifestations. 6 references. (Author abstract)

172114 Kales, Anthony; Bixler, Edward O.; Tan, Tjiauw-Ling; Scharf, Martin, B.; Kales, Joyce D. Sleep Research and Treatment Facility, Milton S. Hershey Medical Center, 500 University Dr., Hershey, PA 17033 **Chronic hypnotic-drug use: ineffectiveness, drug-withdrawal insomnia, and dependence.** Journal of the American Medical Association. 227(5):513-517, 1974.

The effects on sleep patterns caused by the chronic use of hypnotic drugs were studied. Ten patients with insomnia, each of whom had been using hypnotic drugs for periods ranging from months to years, were monitored in a sleep laboratory while continuing to receive medication. A comparison with insomniac controls who were not receiving medication demonstrated a significant decrease of rapid eye movement (REM) sleep in the chronic drug users. These patients also had as great or greater difficulty in falling asleep or staying asleep, or both, than the insomniac controls. It is concluded that the ineffectiveness of hypnotic drugs demonstrated in this study and in earlier sleep laboratory evaluation studies indicates the need for changes in the guidelines used for evaluating and advertising hypnotic drugs. 14 references. (Author abstract modified)

172992 Wilson, Ian C.; Prange, Arthur J., Jr.; Lara, Patricio P. Dorothea Dix Hospital, Raleigh, NC 27611 **Methyltestosterone with imipramine in men: conversion of depression to paranoid reaction.** American Journal of Psychiatry. 131(1):21-24, 1974.

Five men with primary unipolar depression were treated with methyltestosterone and imipramine. Four promptly showed a paranoid response that cleared rapidly when treatment with the hormone was discontinued. It is suggested that the shift from depression to a paranoid reaction may have resulted from an increase in aggression, which may in turn have been the result of the interplay between the hormone and the drug and the effects of this interplay on brain biogenic amine metabolism. 26 references. (Author abstract)

173080 Lee, Kil Hong; Cho, Yong Nam. Dept. of Neuropsychiatry, Medical College, Woo Sok Univ., Korea **Studies on side effects and withdrawal symptoms of iminodibenzyl derivatives.** Neuropsychiatry (Seoul). 9(2):115-121, 1970.

Clinical studies of the side effects and withdrawal symptoms of the iminodibenzyl

derivatives administered to 100 depressive patients, diagnosed and treated during a 2 year period were reported. Among the side effects noted were: varied symptoms of the autonomic nervous system; oral dryness; constipation; poor appetite; blurred vision; general weakness; dizziness; headache; difficult urination; palpitation; bad taste; epigastric pain and drowsiness. Withdrawal symptoms included perspiration, chilling, nausea, mild fever and vomiting. The incidence of side effects for imipramine withdrawal was less than that of amitriptyline alone or of the combination of imipramine and amitriptyline. 13 references. (Journal abstract modified)

173866 Johnson, D. A. W. University Hospital of South Manchester, South Manchester, England **The psychiatric side-effects of drugs.** Practitioner (London). 209(1251):320-326, 1972.

Drugs prescribed for various physical conditions are discussed in relation to their side-effects on the mental functioning or affective state of the user. It is suggested that the possible psychiatric effects of drugs should be more carefully considered, both in the prescribing of drugs and in considering the etiology of any psychiatric illness arising in a physically ill patient. Specific effects of various classes of drugs are described. (Author abstract modified)

174297 Miller, Edith Maria; Neiburg, Herbert A. Maimonides Medical Center, 4802 10th Ave., Brooklyn, NY 11219 **L-Tryptophan in the treatment of levodopa induced psychiatric disorders.** Diseases of the Nervous System. 35(1):20-23, 1974.

The rationale for treatment with L-tryptophan in levodopa disorders is investigated. Nine patients with levodopa induced psychiatric side-effects were treated with L-tryptophan in a single-blind controlled study. In all patients levodopa therapy was continued and no sedative agents were given. In eight patients all psychiatric side-effects cleared within 48 hours; there was no reoccurrence of these symptoms on an 8 month followup. Six patients with levodopa induced psychiatric disorders were used as control subjects and not treated with L-tryptophan. In these patients mental changes subsided only after levodopa had been discontinued for a period of 2 to 8 weeks. This study confirms the results described by Dr. Birkmayer, who treated levodopa induced psychosis first in 1972. 20 references. (Author abstract modified)

174561 Barraclough, B. M. Clinical Psychiatry Unit, Graylingwell Hospital, Chichester, Sussex, England **Are there safer hypnotics than barbiturates?** Lancet (London). 1(7846):57-58, 1974.

The mortality associated with prescribing barbiturates, barbiturate containing ipecacuanha and nitrazepam is assessed. Over the 6 years, 1965-1970, the number of deaths in which these drugs were implicated and the death rate per million prescriptions for each drug were 12,354 and 133 for barbiturates, one and nine for barbiturate containing ipecacuanha, and 90 and 13 for nitrazepam. Evidence suggests that nitrazepam is a safer drug than barbiturate. No definite conclusion can be reached about the safety of barbiturate containing ipecacuanha. It is felt that prescribing safer hypnotics and sedatives than barbiturates may make overdoses less likely to be fatal. Large differences in death rates suggest that both barbiturates and nitrazepan are less lethal than barbiturates in clinical practice. A feature of nitrozepam which may contribute to its safety is the bulky tablet of the commonly prescribed 'Magadom,' which makes the swallowing of overdoses hard work. 5 references. (Author abstract modified)

174784 Amielanczyk, Wladyslaw. Elblag, ul. Diaczenski 8 m 6, Poland **/Delirious syndrome after the administration of haloperidol./** Zespol majaczeniowy po podaniu haloperidolu. Psychiatria Polska (Warszawa). 7(2):219-221, 1973.

Results of treating a 22-year-old schizophrenic soldier with other neuroleptics before continuing with haloperidol in 5mg doses are described. Haloperidol, a butyrophenon derivative, is a strong neuroleptic that lowers the contents of 5-hydroxytryptamine and catecholamine in the brain. It is used in states of motor excitement, in paranoid and catatonic schizophrenia, and in manic states. Its primarily extrapyramidal side-effects have been described, but no cases of mental disorders attributable to the drug have been reported. In this case the patient developed a delirious state within 30 minutes after the first intake (tongue extruded, tense extremities, shouting unintelligible remarks, and other symptoms) but the state responded satisfactorily to treatment with scopolamine. 5 references. (Author abstract modified)

174966 Scott, Jean Eastwood. University of California, Los Angeles, CA **Phenothiazines-contraindicated for the underfat. (Dr.P.H. disserta-**

tion). Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-1730 HC$10.00 MF$4.00 110 p.

The relationship of body lipids to the analysis and treatment of mental health problems is investigated in a carefully selected patient population on whom body fat could be accurately determined. The underfat did less well with hospitalization and treatment than did the normally fat or overfat. Underfat patients treated with phenothiazine derivatives, a highly lipophilic family of drugs, did less well than did the normally fat or overfat. There was no statistical relationship between fatness and outcomes among patients who were not treated with a phenothiazine derivative. Speculations concerning an improvement in the effectiveness of the phenothiazine derivatives are presented. (Journal abstract modified)

16 METHODS DEVELOPMENT

168804 Ban, T. A.; Lehmann, H. E. Div. of Psychopharmacology, Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **Systematic clinical studies with trazodone: methodological aspects.** Current Therapeutic Research. 15(10S):764-768, 1973.

Some methodological aspects of systematic clinical studies with trazodone are reported. The clinical investigations of the triazolo - pyridine compound were conducted on 25 human Ss given doses of trazodone orally and exposed to a battery of perceptual, psychomotor and attention tests; systematic; clinical, in which the range of therapeutic activity of trazodone was explored; and documentation, in which two independent systems (in North America and in Europe) were developed for the documentation of clinical psychotropic drug trials. Suggestions for future research are included. 2 references.

169673 Garrett, Edward R. College of Pharmacy, Box 779, J. Hillis Miller Health Center, University of Florida, Gainesville, FL 32610 **Stability and microanalysis of tetrahydrocannabinol.** Final Report, NIMH Grant MH-19268, 1973, 48 p.

A study of the stability and microanalysis of tetrahydrocannabinol (THC) is presented in which an analytical method, based on gas chromatographic analysis of derivatized THC, developed to permit the assay of THC in biological fluids at the sensitivity that permits the monitoring in blood of THC for 10 hours after smoking one valid marihuana cigarette is described. A method of variable plasma concentrations was devised so that protein binding was determined from the pseudoplasma concentrations of drug after the separation of the pseudoplasma from the red blood cells added to form pseudoblood with known concentrations of delta9-THC. This use of the competition between the high partitioning of drug between red blood cells with plasma water and the binding to plasma protein permitted an estimate of 97% blinding which was not drug concentration dependent. Small amounts of delta8-THC are produced as are two gas chromatographically observable products and the rate of their appearance appears to parallel the rate of delta9-THC degradation. 21 references.

171630 Glenne, P. O.; Pilbrant, A.; Sundwall, A.; Vessman, J. Research Department of the KABI Group, S-104 25 Stockholm, Sweden **Relationship between bioavailability and dissolution rate of oxazepam.** Acta Pharmacologica et Toxicologica (Kobenhavn). 31(Supplement 1):90, 1972.

At the 25th meeting of the Scandinavian Pharmacological Society, the relationship between bioavailability and dissolution rate of oxazepam was reported. Five oxazepam formulations with differing in vitro dissolution rates were given, in partial cross-over fashion, to a panel of healthy volunteers. After the absorption profiles were determined, an in vitro dissolution rate method, which correlated with the absorption profiles, was worked out. The dissolution rate profiles were changed by varying the stirring rate. When the correlation once is established a cheap in vitro dissolution test gave meaningful information about the in vivo performance of every manufactured tablet batch. (Author abstract modified)

172397 Goenechea, S.; Brown, S. S.; Ferguson, M. M. Institut fur Gerichtliche Medizin, D-5300 Bonn, Stiftsplatz 12, Bundesrepublik Deutschland **/Gas chromatographic determination of methaqualone in small amounts of serum after ingestion of therapeutic doses./** Gaschromatographische Bestimmung von Methaqualone in kleinen Mengen Serum nach Einnahme therapeutischer Dosen. Archiv fur Toxikologie (Berlin). 31(1):25-30, 1973.

Serial plasma methaqualone levels have been determined in normal fasting subjects after therapeutic doses of each of three preparations of the drug. Peak levels were reached within 1 to 2 hours, with a subsequent rapid fall, and the data

indicate that the hydrochloride of methaqualone is more quickly absorbed than the base. 14 references. (Author abstract)

172398 Norheim, Gunnar. Rettsmedisinsk institutt, Rikshospitalet, Oslo 1, Norway **Determination of doxepin in autopsy material.** Archiv fur Toxikologie (Berlin). 31(1):7-12, 1973.

A case of doxepin intoxication is reported. Relevant autopsy findings are mentioned and an extraction procedure for the determination of doxepin in autopsy material is described. UV spectrum, gas chromatography data, infrared and mass spectra of doxepin are given. Thin layer chromatography of urine extracts gave three metabolites. These are not yet identified. The results of the toxicological investigations are presented. 6 references. (Author abstract)

173307 Priest, R. G. St. George's Hospital Medical School, London, S.W. 17, England **The design of therapeutic trials: a critical analysis with illustrations, particularly from the field of psychotropic drugs or: why no one can ever do a proper drug trial.** Psychotherapy and Psychosomatics (Basel). 22:172-175, 1973.

A critical analysis of the design of therapeutic trials is presented with illustrations, particularly from the field of psychotropic drugs. Problems in the design of drug trials are discussed in terms of incompatible methodological requirements. Examples are presented which illustrate that there is no possible right number of patients for a drug trial, no right place to perform a trial, no right dosage scheme, no ideal patient to use in trials, and no standard formula for determining the amount of information to record on each patient. (Author abstract modified)

174135 Serafetinides, E. A.; Willis, D. Department of Psychiatry, School of Medicine, University of California, Los Angeles, CA 90024 **A method of quantifying EEG for psychopharmacological research.** International Pharmacopsychiatry (Basel). 8(4):245-247, 1973.

A method of quantifying EEG for psychopharmacological research is discussed. An experiment is described which illustrates that both subjective impressions on EEG correlates of psychopathology and severity of illness can be quantified. It is suggested that with this new insight on the biological aspects of mental illness can be achieved. 3 references. (Author abstract modified)

174853 Fukumoto, Mamoru; Sawada, Hideo; Hara, Akira. Dept. of Legal Medicine, Gifu University School of Medicine, Gifu, Japan **Semiquantitative analysis of bromazepam by ring oven method.** ACTA Scholae Medicinalis Universitatis in Gifu (Gifu). 20(6):600-607, 1972.

A new procedure for the semiquantitative assay of bromazepam was developed involving the chromatography by ring oven method and the colorimetric measurement by the color compound formed with iron. The obtained ring on the filter paper was compared with that of the authentic bromazepam and applied to the identification of bromazepam itself in blood of animals. The adopted procedure utilized the ring oven response to the small amounts of the identification of bromazepam and was applied to the determination of bromazepam and its major metabolites in blood and urinary excretion of humans and animals. 8 references. (Author abstract modified)

17 MISCELLANEOUS

167382 Pearlman, Samuel; Silverman, Irving. Brooklyn College, City University of New York, Brooklyn, NY **The role of research in drug abuse intervention: street drug analyses.** Drug Forum. 2(3):227-237, 1973.

Analyses of street drugs illicitly distributed show adulterations and substitutions of psychoactive drugs. Consideration is given to whether such reports can be used in educational programs with drug users and others to offset partial failure of present drug education attempts. The role of the researcher in drug intervention programs is discussed. 17 references.

167585 Fejer, Dianne; Smart, Reginald. Addiction Research Foundation, Toronto, Ontario, Canada **The use of psychoactive drugs by adults.** Canadian Psychiatric Association Journal (Ottawa). 18(4):313-320, 1973.

A survey of psychoactive drug use among 1200 adults in Metropolitan Toronto is reported. Data indicated that 23.8% of the sample had at least one prescription for psychoactive drugs in the last year; most with prescriptions were females. Young persons (18 to 19 years old) had fewer prescriptions than those over 60. The types of drugs used are presented and associated with the population groups which use them most frequently. Physical and mental health characteristics of drug users are also included. 12 references.

167706 Leeds, Alice A. NIMH, 5600 Fishers Lane, Rockville, MD 20852 **International Reference Centers Network for psychotropic drugs.** In: Brown, B., International collaboration in mental health. Rockville, Md., NIMH, 1973. 291 p. (p. 26-31).

Since 1967 NIMH has been involved in a joint program with the World Health Organization to set up and operate an international network for the collection and dissemination of information on drugs used in the treatment of mental diseases. One of the aims of the International Reference Centers Network is to insure that psychiatrists become aware as rapidly as possible of the therapeutic action as well as the concomitant effects of psychotropic drugs. NIMH and WHO projects in this area are discussed. (Journal abstract modified)

168272 Ogawa, Nobuya. Kyushu University, Japan **Behavioral pharmacology.** Kyoiku to Igaku (Fukuoka). 20(8):748-754, 1972.

Screening tests of psychotropic drugs in behavioral pharmacology are discussed. The method of testing drugs by comparing between general and pharmacologically induced behavior is examined. Aggressive behavior and pharmacologically induced calm behavior are compared. The methods of testing inactivating action in drugs toward conditioned behavior, spinal reflex, anticonvulsive action, katalepsia inducing action, and antidepressant action are considered.

168302 Adachi, Keiko; Shibata, Yukiko. Asahigawaso, Okayama, Japan **Current situation of the use of drugs in Asahigawa Jido-in.** Annual Report of Asahigawaso (Okayama). 4(2):37-40, 1972.

The use of drug therapy during 1971 at the Asahigawa institution for children is examined. Types of drugs used included: phenobarbital, diphenylhydantion, carbamazepine, primidone, diazepam and nitrozepam. The budget for drugs at the instituion accounted for 52.1% of the entire yearly expenditure.

168312 Stancer, Harvey C. University of Toronto, Toronto, Ontario, Canada **Yesterday, today and tomorrow: a point of view.** Canadian Psychiatric Association Journal (Ottawa). 18(5):371-376, 1973.

A review of research in the field of psychopharmacology is presented, showing how its first serendipitous steps are evolving into enquiries of where and how drugs work. The discovery of the clinical use of phenothiazines as antipsychotic agents, as well as imipramine and iproniazid as antidepressants, theories explaining the use and operation of these drugs, and the issue of prevention of disorders are examined. Megavitamin therapy, or the use of nicotinic acid combined with a number of other vitamins, is examined as offering hope to families with members suffering from schizophrenia. The advent of social therapies in psychiatry has been heralded as a third revolution. The problem of unbiased, independent funding for psychopharmacological research is discussed. These areas of concern in the field are summarized by indicating possible directions for the future. 38 references.

168361 Pope, Frederick E. Honolulu, HI **Should we put benzodiazepines in our drinking water?** Hawaii Medical Journal. 32(5):323-324, 1973.

Benzodiazepines are discussed with emphasis on their use and function. The benzodiazepines discussed are chlordiazepoxydihydrochloriodum (Librium), chlorazepanum (Tranxene), diazepamum (Valium), and ozazepamum (Serax). Physiologically, the mode of action is predominantly subcortical. Small amounts of benzodiazepines are specific blockers of the limbic system and therefore also influence the reticular system and reticular formation of the brain stem. However, huge doses are necessary to depress cortical structures for a desired therapeutic effect. The four main functions of benzodiazepines are anxietolytic, sedative, muscle relaxant, and anticonvulsive. The half-life of these drugs is long, and the patient should be clean before anticoagulants are given. These drugs should not be given to patients with myasthenia gravis. As far as side-effects are concerned, these drugs are relatively safe. However they should be used with caution with patients who drive, drink alcohol, or have an organic disease causing physical fatigue. 1 reference.

168800 Vinar, O. Institute of Psychiatry, Prague, Czechoslovakia **Introductory remarks: new agents in psychiatry.** Current Therapeutic Research. 15(10S):743-744, 1973.

The introduction of and use of new psychotropic drugs in psychiatry is examined and comments on well established principles for decisions about accepting a new drug are included. It is felt that a new drug should not only be more effective than a placebo but it should be better than other drugs of its kind currently on the market. The new drug should be therapeutically superior to standard treatment. At the present time, this requirement is not forced on the manufacturer of drugs. 2 references.

169748 Klerman, Gerald L. Psychiatry Service, Massachusetts General Hospital, Boston, MA 02114 **Psychotropic drugs as therapeutic agents.** Lex et Scientia. 9(4):110-131, 1972.

The range of psychotropic drugs available for therapeutic use and the state of knowledge as to their known clinical utility are reviewed. These include the antipsychotic drugs, such as phenothiazines, thioxanthines, rauwolfia derivatives, butyrophenones and benzoquinoline; the antidepressants, such as psychomotor stimulants, MAO inhibitors, and tricyclics; and the antianxiety drugs, such as sedative-hypnotics, meprobamate, and diazepoxide. The availability of large numbers of these compounds has not only benefited the patients, but also brought psychiatric practice closer to the medical model. Scientifically important consequences have been generated for increased sophistication in research methodology for testing and evaluating these drugs both in animals and humans, but even more important social and moral questions have been raised by their increased use. Such issues include the right to treatment in this manner, the dilemmas of involuntary treatment of mental disorders by drugs or other techniques, the emergence of new forms of social disability and chronicity for mental patients released into the community due to successful drug treatment; and the question of whether or not we are becoming an overmedicated society.

169945 Deniker, P.; Ginestet, D. Faculte de Medecine de Paris, Centre Psychiatrique Ste. Anne, 1 rue Cabanis, Paris, France **/Psychopharmacology of old age./** La psychopharmacologie de la vieillesse. Giornale di Gerontologia (Firenze). 20(10):965-975, 1972.

Experience in treating patients over 60 in hospitals is outlined, and indications for use of the major categories of psychotropic drugs, including psycholeptics, sedatives, including hypnotics, tranquilizers, neuroleptics, and the energizers of mind and mood, are described and tabulated. The problems encountered in the use of new drugs, and the psychopharmocological research required in connection with the old ones, are detailed. Good results have been obtained in anxiety cases, and cautious use of thymoanaleptics has benefited those suffering from depression. Ambulatory care is more frequent and useful in modern therapy, making it possible to maintain the elderly in their social and domestic environment to an increasingly greater extent. 4 references.

170754 Nakajima, Hiroshi. Nippon Roche Research Center, Office No. 883, Kokusai Bldg., Marunouchi 3-chome, Tokyo, Japan **Clinical research aspects of psychotropic medication.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):168-206, 1970.

Clinical studies in humans on aspects of psychotropic drugs covering toxicology, phar-

macology, research design and organization are discussed. Special aspects of the clinical study of psychotropics involve the following factors: unknown etiology, no uniformity in classification, lack of epidemiological studies/data, difficulty in qualitative and quantitative measurements of psychic phenomena factors, influence of society and environment, and the ethics of human experimentation. The factors that modify the effects of psychotropic drugs are of importance to the patient, the doctor or therapist, and to the environment. 21 references.

170802 Sheerin, Elizabeth. Division of Health Education, N.S.W. Health Commission, Mena House, 225 Macquarie Street, Sydney, N.S.W. 2000 **A programme which led to reduction in night sedation in a major hospital.** Medical Journal of Australia (Sydney). 2(14):678-681, 1973.

A considerable decrease in the consumption of night sedation and the abolition of night sedation rounds was the result of a drug education program at a major Sydney hospital. The program consisted of one day seminars for the staff, where talks of pharmacology, drugs in the hospital context, crisis theory, alcoholism and drug dependence were presented. These were followed by small discussion groups which formulated recommendations for changes in routine hospital practices, thereby reducing the use of sedatives. 5 references.

170847 Roscam Abbing, P. J. no address /**Effect and aftereffect of drugs: ethical considerations on the use of psychotropic agents (1).**/ Werking en nawerking van drugs. Ethische beschouwing over het gebruik van bewustzijnsbeinvloedende middelen (1). Intermediair. 7(27):1, 3, 5, 11, 1971.

Ethics of using psychotropic drugs are discussed in terms of their effects and aftereffects. When an artificial state of euphoria is created through drugs, it is felt that the persons has become the victim of a specific action; he is no longer free.

171121 Bayulkem, Faruk. Bakirkoy Nevro Psychiatry Hospital, Istanbul, Turkey **Drugs and psychiatric readaptation.** Israel Annals of Psychiatry and Related Disciplines (Jerusalem). 11(2):108-111, 1973.

Drugs and their effects on psychiatric readaptations are discussed. It is suggested that treatment of the mentally ill is highly successful compared to 10 years ago, and that medicine plus rehabilitation makes the successful results even higher. It is contended that classification according to various clinical pictures and symptomology and specific psychiatric rehabilitation cannot be defined as yet. It is concluded that readaptational programs should not be based on the principles which aim to correct the personal behavior of the patient alone, but should be designed so that every possible adaptation difficulty which may occur in the patient's relations with his family and society could be corrected. (Author abstract modified)

171159 Kim, Sang Tae. Chungryangri Mental Hospital, Seoul, Korea **About the psychotropic drugs.** Journal of the Korean Medical Association (Seoul). 16(2):121-128, 1973.

Classifications of psychotropic drugs are presented in tables that present their effects and indications. A summary of the pharmacological observations consistant with the catecholamine hypothesis of affective disorders is reported. Dosages of hypnosedatives, major tranquilizers and psychostimulants are presented along with their side-effects. 9 references.

171257 no author. no address **Drugs commonly used in mental conditions.** Medicine and Surgery (Bombay). 11(11):40, 1971.

Twenty eight drugs most commonly used in mental conditions are listed. They are subdivided into three groups: psychosis excitements, neurosis, and controlling extrapyramidal symptoms. They can be used for acute excitements, withdrawal, depression, anxiety states, hysterical fits, etc. Meprobamate, eskazine, siquil, and calmpose are included in the list. Various dosages are also given for each treatment.

171485 Singer, K. Dept. of Psychiatry, Univ. of Hong Kong, Queen Mary Hospital, Hong Kong **Psychotropic drugs in medical practice.** Bulletin of the Hong Kong Medical Association (Hong Kong). 24(1):103-115, 1972.

The uses and adverse reactions of psychotropic drugs of the following types are summarized: antipsychotic drugs, such as phenothiazines, butyrophenones, and thioxanthenes; antianxiety drugs, such as minor tranquillizers, hypnotics, and sedatives; and antidepressant drugs, such as tricyclic antidepressants, monoamine oxidase inhibitors, and psychostimulants. The hallucinogens are excluded. The greatest value of psychotropic

drugs is in the treatment of schizophrenia. The results of drug therapy have been less satisfactory in the treatment of depression and least for anxiety and psychosomatic conditions, although, when used with discrimination, they can provide much symptomatic relief. The conclusion is that knowledge of the use and adverse effects of psychotropic drugs enables the physician to treat more effectively the majority of neuroses and psychosomatic conditions with which he now deals in the community.

171568 Editorial Board. Hong Kong Journal of Mental Health, Hong Kong **Common psychotropic drugs.** Hong Kong Journal of Mental Health (Hong Kong). 2(2):2-4, 1973.

The commonly used psychotropic drugs are reviewed. The uses, toxicology, chemistry and side-effects are briefly examined. Included are: 1) major tranquilizers (phenothiazine derivatives and butyrophenones); 2) minor tranquilizers (meprobamate, chlordiazepoxide, diazepam); 3) antidepressants (monoamine oxidase inhibitors, tricyclic compounds) and 4) stimulants and psychotomimetic drugs.

172109 Kramer, John C.; Pinco, Robert. Dept. of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Amphetamine use and misuse with recommendations for stimulant control policy.** Journal of Psychedelic Drugs. 5(2):139-145, 1972.

Uses and misuses of amphetamines are reviewed along with a history of the nation's drug control policy. Legitimate uses of amphetamines are for obesity, mild depression, hyperactivity, and narcolepsy. The abuse of amphetamines could lead to violence. The moderate prescription restrictions placed on physicians in the mid-Sixties proved ineffective in reducing or eliminating massive diversions and overprescribing. Because of public pressure in the late 1960's and early 1970's, Congress and the Bureau of Narcotics and Dangerous Drugs severely restricted production and distribution throughout the legitimate drug industry. 20 references.

172809 Oeripsantoso, Sardjono. Department of Pharmacology, University of Indonesia, Djakarta, Indonesia **Some aspects of psychotogenic drugs.** Indonesian Psychiatric Quarterly (Djakarta). 4(3):5-13, 1971.

Aspects of psychotogenic drugs are briefly reviewed. The use of these drugs, especially marihuana, for therapeutic purposes has been replaced by other therapeutic agents which are more potent and effective. These drugs are now mainly used for research purposes. The abuse of these agents among teenagers for decreasing or repressing psychological problems and other reasons is also discussed; a psychiatric case with a habit of taking marihuana to decrease and repress his psychological problems is presented. Whether a correlation exists between the agent and the mental disturbance is not known. However, the psychotogenic drug might be a precipitating factor. Although these drugs do not cause dependence, efforts to prevent the abuse of these agents are urged. The roles of physicians, psychiatrists, psychosociologists and parents are very important. 11 references. (Author abstract modified)

173452 Vinding, Terkild. Saint Albans Hospital, Radford, VA **Impressions of Scandinavian psychiatry -- 1973.** Journal. 5(1):28-29, 1973.

Impressions gained during a visit to several Scandinavian psychiatric centers are discussed. Treatment programs are surprisingly uniform in Norway, Denmark and Sweden; psychotherapy, individual and group, drug therapy, ECT, physiotherapy, vocational rehabilitation and family therapy are in use. Phenothiazines, butyrophenones, antidepressants are used extensively. Electroshock is used sparingly. The old barbital treatment of alcoholism is still in use. Lysergic acid diethylamide is used far less in hallucinogenic drug therapy due to abuse and its 8 hour action. Instead, psilocybin, CI 39, CEY 19 and CZ 74, effective for about 3 hours, are used. Treatments are preceded by a period of several weeks in which the patient participates in group therapy and is introduced to a daydream technique which will be intensified when hallucinogenic drugs are introduced.

174618 Sadono, B. Department of Psychiatry, Faculty of Medicine, University of Indonesia, Djkarta, Indonesia **Psychotropic medication in Indonesia (1970-1973).** Indonesian Psychiatric Quarterly (Djkarta). 6(3):53-65, 1973.

The use of psychotropic medication in Indonesia is discussed. Clinical drug trials were carried out in a number of centers. The results are summarized according to categories of major tranquilizers, minor tranquilizers, and antidepressants.

Policies of the directorate of mental health and the ministry of health are reviewed. 18 references.

174641 Woolley, E. St. Edward's Hospital, Cheddleton, Staffordshire, England **Polly: mental deficiency and schizophrenia.** Nursing Times (London). 69(48):1636-1637, 1973.

A nursing care study concerning the treatment of a 42-year-old woman diagnosed as mentally deficient with schizophrenia is presented. The patient had a history of epilepsy; her behavior in the hospital was at times violent and at other times semistuporose. She also had a recurring skin rash. Her behavior included aggression toward other patients and a variety of self-degrading habits. A detailed description of the psychopharmacological treatment administered is included.

174880 Mouzas, G. L. Emergency and Accident Unit, West Hill Hospital, Dartford, Kent, England **Diazepam used intravenously during reduction of fractures and dislocations.** Practitioner (London). 211(1266):805-808, 1973.

The trial use of diazepam in an accident department where the delay necessary before administration of a general anaesthetic is a marked disadvantage is analyzed. Two hundred six patients (95 females and 111 males) with fractures or dislocations were given either an intravenous injection of diazepam or a general anaesthetic before reduction. Results show that in a busy accident department, the intravenous use of diazepam as sedative cover is a great advantage both to the doctor and the patient. The operator (doctor) can proceed immediately with treatment, while waiting time for patients is reduced, side effects are few, and there is no loss of consciousness. Diazepam is considered to be preferable to local anaesthesia as the latter is frequently insufficient to obtain a perfect reduction. 6 references.

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